PITT STREET RESEARCH

Anatara Lifesciences

Following the gut

Share Price: $0.36

ASX: ANR

Sector: Healthcare

14 March 2019

The Anatara/Zoetis deal is a company maker

Anatara Lifesciences, a Melbourne-based drug developer focusing on GI therapies, partnered with Zoetis in an exclusive worldwide licensing agreement for its lead drug, bromelain-based Detach, in May 2018. We believe that the opportunity is remarkable, given the size and scale of Zoetis' animal health portfolio. Considering the wide manufacturing, marketing, and distribution network of Zoetis, the company is expected to be able to contribute more effectively to Detach's development than Anatara could have (it being a small company). The deal is also extremely momentous for Anatara, as the interest from one of the largest animal health companies worldwide reaffirms the credibility of the bromelain technology and reduces Anatara's cost burden, while providing a stream of cash flow to help the company move forward with its plans in human GI health.

Upside from a human health application

Anatara is now focusing on developing a bromelain-based **Ga**strointestinal **Re****P**rogramming (GaRP) product, for human GI health, particularly in irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). The product is being positioned as a dietary supplement that could be used by itself or in conjunction with prescription medications. Due to the regulatory and commercial advantages associated with natural products and the complexity of management of these diseases, we believe GaRP has a significant upside potential.

Additionally, considering the excellent safety and efficacy profile of Detach, the product is expected to witness a rapid adoption, especially on the back of Zoetis' global presence. Anatara's current cash is sufficient to fund GaRP in the human GI space through to the point of licensing out. Milestones and royalty payments will provide funding for future developments.

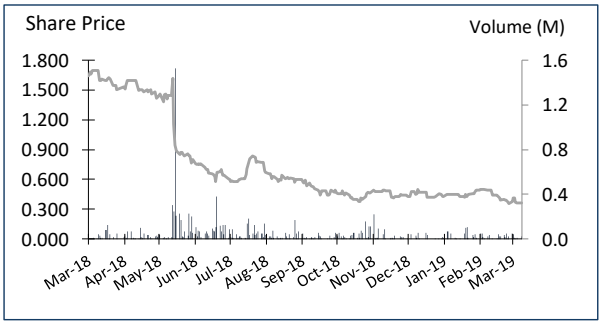
Valuation

We value Anatara at $1.34 per share base case and $3.61 optimistic case using a probability-weighted DCF valuation approach. Anatara is currently trading way below this valuation range. We see the potential to be re-rated by the market as GaRP progresses and as Zoetis gains regulatory approvals and launches Detach in North America, Europe and Asia.

Market Cap. (A$ m)	17.8
# shares outstanding (m)	49.4
# share fully diluted	51.0
Market Cap Ful. Dil. (A$ m)	18.4
Free Float	100%
12 months high/low	$1.70 / $0.36
1 / 3 / 12-month performance	-28% / -19% / -79%
Website	anataralifesciences.com

Source: Company, Pitt Street Research

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



Source: FactSet, Pitt Street Research

Valuation metrics	
DCF fair valuation range (A$)	1.34 / 2.47
WACC	15%
Assumed terminal growth rate	None

Source: Pitt Street Research

Subscribe to our research HERE

Analyst: Stuart Roberts

Tel: +61 (0) 447 247 909

Stuart.roberts@pittstreetresearch.com

Table of Contents

Introducing Anatara Lifesciences (ASX: ANR)

Anatara Lifesciences, a Melbourne-based drug developer, is focusing on development of a natural compound called bromelain for gastrointestinal (GI) diseases in animals and humans. Its lead product, a bromelain formulation called 'Detach', is a non-antibiotic solution to control diarrheal disease (known as scour in livestock). The product has already been exclusively licensed to Zoetis[1] for worldwide development, manufacturing, distribution, and marketing, for use for livestock and horses. Anatara is presently working on developing proprietary bromelain formulations for gastrointestinal conditions in humans, including Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD) through its new bromelain-based product candidate 'Gastrointestinal ReProgramming (GaRP)'.

What is bromelain and how is Anatara using it?

Anatara is re-strategizing its focus to explore the use of bromelain in human GI health

First introduced as a therapeutic compound in 1957, bromelain is a mixture of proteases obtained from the fruit or stem of pineapples. These proteases have anti-attachment, anti-secretory, and anti-inflammatory properties. Over time, scientists have identified numerous potential therapeutic applications of bromelain in conditions as diverse as osteoarthritis, angina, and cancer[2].

Anatara is using bromelain to focus on two areas – antimicrobial resistance and gut health. Diarrhea-causing bacteria have the potential to cause disease once they attach themselves to various receptors located on the intestinal mucosa. Bromelain prevents these bacteria from attaching, thus rendering them harmless. Interestingly, this mechanism of action overcomes issues related to antibiotic resistance in animals as it does not kill the bacteria, but only prevents their attack.

The properties of bromelain that make it useful for potential exploration in gut health include its Generally Recognized as Safe (GRAS)[3] status which allows it to be used as a food additive. Moreover, it has been used as an anti-inflammatory and anti-cancer complementary medicine in the US and the EU and where its unlimited daily intake acknowledges its excellent safety profile. These evidences rationalize its potential use in human as well as animal health.

Which bromelain-based products is Anatara developing?

Anatara's first veterinary product, Detach, leveraged several of bromelain's biological activities, that is, its ability to reduce the attachment of pathogenic bacteria to the gastrointestinal tract and down-regulate fluid secretion that results in diarrhea. The original formulation of bromelain, also called Detach, was developed in the late 1980s and early 1990s for use in the animal health market[4]. Anatara developed a new formulation of Detach[5]

Meanwhile, GaRP, Anatara's first human product, exploits the bacterial anti-attachment and anti-inflammatory properties of bromelain while the additional GaRP formulation components contribute to this proprietary product that has been designed to address the disease characteristics of both IBD and IBS. The product is being positioned as an adjunct to prescription

[1] Headquartered in New Jersey, US, NASDAQ: ZTS, www.zoetisus.com.
[2] Biotechnol Res Int. 2012;2012:976203. Epub 2012 Dec 10.
[3] Under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act (the Act), any substance that is intentionally added to food is a food additive, and is subject to premarket review and approval by FDA, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use.
[4] *See Use of enzymes, especially bromelain, in the treatment of diarrhoea, WO/1994/000147, priority date 30 June 1992, invented by Tracey Mynott.*
[5] *The current Detach formulation, developed shortly after the 2010 startup of Anatara and patent protected from 2014, differs from its predecessor in that it does not contain phthalates – excipients now no longer used due to their potential toxicity (for background on this see Phthalates are everywhere, and the health risks are worrying. How bad are they really? Amy Westervent, The Guardian, 11 February 2015.*

drugs in active disease or as a maintenance therapy when patients enter remission. The GaRP dietary supplement proof-of-concept studies in animal models have completed with favourable results - in industry-standard *in vitro* gut models, Anatara has been able to show that GaRP can:

- reduce production of pro-inflammatory proteins by gut and inflammatory cells by >85%;
- reduced the attachment and invasion of IBD and IBS pro-inflammatory bacteria into healthy gut cells by >95%;
- Protect and maintain gut integrity.

What is the rationale of developing Detach and GaRP for potential use in animal and human health, respectively?

Following extensive safety and efficacy trials, Anatara received APVMA approval for the product in Australia for piglets in October 2018. The product has been successfully out-licensed to Zoetis and hence the company has moved on to explore potential human uses of bromelain-based products.

GaRP is being positioned as a dietary supplement for management of IBD and IBS

Anatara's first product candidate for human health – GaRP – is being positioned as a dietary supplement for the management of IBD and IBS. Both diseases exhibit shared characteristics such as an altered microbiome, impaired intestinal barrier function, mucosal damage and various levels of inflammation. These disorders are currently treated with anti-inflammatory medications or a range of prescription medicines aimed at treating symptoms. However, these therapies are associated with high treatment failure rates which have resulted in a significant unmet therapeutic and market need. GaRP could potentially fill the gap in the GI therapeutics market as it has been designed to restore homeostasis of the gut microbiome, reduce inflammation, and repair mucosal damage, thus overcoming the collective disease characteristics associated with gastrointestinal conditions. Moreover, the company believes that GI disorders represent a lucrative market, since increased education and detailed evaluation of dietary supplements has led healthcare providers to include dietary supplements in the symptom management of both IBD and IBS.

Why did Anatara out-license Detach to Zoetis?

In May 2018, Anatara announced the out-licensing of Detach to Zoetis for worldwide development, manufacturing, distribution, and marketing of the drug for livestock animals and horses for A$2.5m in upfront payment and milestone payments of up to A$6.3m. Royalty rates on product sales typically range 3–4%. However, the intellectual property (IP) licensed to Zoetis under the agreement is expected to remain the sole property of Anatara. Through this deal, Anatara is expected to remain well-funded with no loan facilities or liabilities. We believe the company has sufficient funds required to achieve its milestones for human product development through 2020. By then, the company expects to be able to find suitable partnering and/or licensing arrangements.

Nine reasons to look at Anatara Lifesciences

1) **Anatara has been able to out-license Detach to one of the largest animal health companies globally.** Zoetis has annual revenue of US$5bn, two-thirds of which is derived from farm animal health products. Moreover, the firm has a much wider scale of manufacturing, marketing, and distribution network compared with Anatara. Therefore, this is an overwhelming opportunity that will help drive the commercialization of Detach worldwide. Moreover, the deal establishes the credibility of Anatara's bromelain technology and bodes well for future partnership deals of products based on this technology.
2) **Detach is likely to remain attractive amid concerns regarding antibiotic resistance.** The rising incidences of drug-resistant bacteria or 'superbugs' globally have been a cause of worry for policy-makers and food producers alike, with many key opinion leaders advocating for lower use of antibiotics in the food chain. This adds to the lucrativeness of Detach as replacement to antibiotics while still preventing infectious diseases of production animals.
3) **Detach has a long history of development and has shown strong results in piglets.** Detach has been studied since the 1980s and has shown significant reduction in mortality and increase in weight of pigs in Australia and the EU. In fact, it has already received APVMA approval for commercialization in Australia. Although Anatara does not have any say in the product development after it out-licensed the product to Zoetis, the company will benefit from the milestone and royalty benefits on Detach's future sales.

Detach has strong results and GaRP's potential market opportunity is significant

4) **Anatara is expected to remain well-funded for the next few years.** Anatara has significant cash, enough to achieve its human GI milestones., The recently executed Detach deal with Zoetis included A$2.5m in upfront payment, milestone payments of up to A$6.3m, and royalties on product sales in the range of 3–4%. Also, the deal reduced cost burden associated with Detach's development and liabilities on Anatara, allowing it to focus completely on other potential indications.
5) **Anatara has a solid management team with significant expertise in human health.** The newly appointed CEO, Steven Lydeamore, has over 25 years of international pharmaceutical experience and deep understanding of the human health space which aligns well with Anatara's long-term objectives. The company has also recently set up a product development advisory board membered by experts in GI health.
6) **There is significant scientific rationale behind GaRP's development in IBD and IBS.** Both conditions are complex to manage, and the currently used prescription drugs have a very high failure rate. Therefore, there is a high unmet need for natural products that can manage symptoms for these chronic disorders.
7) **GaRP has multiple regulatory and commercial advantages.** Since GaRP is being positioned as a dietary supplement (adjunct to prescription medicines), the regulatory pathway to its approval is less stringent compared with pharmaceutical drugs, thus ensuring rapid market entry. Moreover, Anatara benefits from the rising awareness among public and healthcare professionals regarding the use of dietary supplements. The company will also have the strategic advantage of being able to target both consumers and healthcare professionals, increasing GaRP's potential uptake.

8) **The market opportunity in human GI health is significant.** The prevalence of IBD (>5 million sufferers worldwide[6]) and IBS (~11% of the global population[7]) suggests a significant payoff for Anatara should GaRP be able to prove utility in this setting.

9) **Anatara is undervalued on our numbers.** We value Anatara at $1.34 per share base case and $3.61 optimistic case using a probability-weighted DCF valuation approach. Anatara is currently trading way below this valuation range. We see the potential to be re-rated by the market as GaRP progresses in pre-clinical and then in clinical development, and as Zoetis discloses further progress for Detach in field studies and ultimately in regulatory approvals and launches in North America. Europe and Asia.

The Big Picture – Anatara's work on human GI disorders has potential to re-rate the company

After the May 2018 licensing deal to Zoetis, Anatara's share price went down. Basically, the market was disappointed at the apparently low upfronts and milestones that came with the deal and regarded the 3-4% royalty as not a great outcome for the years that Anatara had worked on Detach.

We take a contrarian view on the Zoetis deal. Zoetis is a proven leader in animal health that is hungry to grow with new generation biologicals to replace or augment a lot of the old-fashioned anti-microbials where potentially Zoetis can face a political and regulatory backlash. This means that Detach, once it is launched in all key markets, has the potential to be substantially more than a niche product in the production animal space. In addition, it will not take long for the product to be launched given the lower hurdles required to get the product approved. Consequently, as we show in our valuation section below, we believe that the current Anatara share price is seriously undervaluing the May 2018 deal.

Even if the market ignores Detach, it will be difficult to ignore GaRP. Since the Zoetis deal Anatara has spent a lot of time telling the GaRP story, as a way of emphasizing the versatility of the company's technology base around bromelain and the significant commercial upside from a new product in IBD and IBS. In this note we begin by looking at the GaRP development effort before turning to Detach. We see Anatara potentially re-rating first around good news from GaRP, which can then turn the spotlight on Detach.

Anatara's GaRP opportunity

GaRP is a microbiome-targeted dietary supplement

Anatara's Gastrointestinal ReProgramming (GaRP) product, is a microbiome-targeted multi-component dietary supplement based on bromelain that is being developed to address the primary underlying factors associated with human GI conditions. The product is being positioned as an adjunct to existing prescription medicines, rather than a replacement. Due to the complex nature of GI disorders and diseases coupled with the diversity of individualized symptoms, the failure rate of current prescription therapies is

[6] Source: Crohn's and Colitis Australia
[7] Clin Gastroenterol Hepatol. 2012 Jul;10(7):712-721.e4.

high. Therefore, there is a significant unmet need for products that can manage the chronic symptoms in and underlying causes of GI conditions.

GaRP combines bromelain and other clinically-proven GRAS components to treat GI disorders – some components target the small intestine, while others target the colon. The small intestine-targeted components prevent attachment of pro-inflammatory bacteria, restore gut microbiota, and reduce inflammation. The colon-targeted components, on the other hand, restore gut microbiota, reduce inflammation, regenerate mucosa, rebuild gut integrity which may in turn reduce diarrhea. With its dual targeting approach, GaRP has great potential to have an additive effect on the efficacy of current prescription drugs.

Over the past few years, Anatara has evaluated many potential human applications of bromelain that include inflammation and/or diarrhea including childhood diarrhea, traveler's diarrhea, and diarrhea associated with IBD and IBS. However, recently the company decided to move ahead with exploring bromelain's potential in IBD and IBS[8]. We believe that targeting these indications can bring significant commercial returns to Anatara, based on advantages related to rapid market entry and its competitive edge.

Development of GaRP provides regulatory and commercial advantages to Anatara

Positioning GaRP as a dietary supplement (adjunct to prescription medicines) provides many regulatory and commercial benefits to Anatara. A few of them are outlined below:

- **Less expensive development, less risky path to market, and rapid market entry:** Dietary supplements are regulated differently by the US FDA and are considered to be more like special foods than drugs[9]. Therefore, the regulatory norms for supplements are less stringent which means that the development of GaRP is expected to be cheaper and quicker.
- **Awareness among public and healthcare professionals:** Due to the rising penetration of internet sales[10], increasing disposable income[11], and manufacturers' efforts to raise awareness about their nutritional supplements, consumers have started focusing on their nutritional requirements. Healthcare professionals are also more aware of the benefits associated with the use of supplements as adjunct therapies. Against this backdrop, the market of dietary supplements is quite attractive and the potential uptake of GaRP is expected to be high.
- **Dual target markets:** Dietary supplements can be adopted by healthcare professionals as well as marketed directly to consumers. This provides an advantage of dual market entry strategy to Anatara for GaRP.

GaRP has multiple regulatory advantages and a less risky path to markets

Proof-of-concept studies have confirmed GaRP's potential use in IBD/IBS

Anatara has already completed market feasibility studies, filed a provisional patent application, and completed the dose selection of each formulation component. Anatara completed research to gather *in vitro* data to support GaRP's efficacy in restoring microbiome, reducing inflammation, and

[8] The therapeutic indication was shortlisted by Anatara based on factors including market opportunity, competitive advantage, quality of supporting data, strength of IP protection, and speed to market.
[9] The US FDA regulates dietary supplements under a different set of regulations than those covering 'conventional' foods and drug products. The supplements are covered under the Dietary Supplement Health and Education Act of 1994 (DSHEA).
[10] According to Statista, worldwide internet user penetration is expected to increase from 46.8% (of the total population) in 2017 to 53.7% in 2021.
[11] According to the US Bureau of Labor Statistics, disposable personal income in the US is expected to increase at an annual rate of 4.2% during 2016–2026.

repairing mucosal damage. Over the next few months, Anatara is planning an animal safety study for IBD and a human observational clinical study for IBS.

Figure 1: GaRP's Commercial Development Plan

	2017 H1	2017 H2	2018 H1	2018 H2	2019 H1	2019 H2	2020 H1	2020 H2
Confirmed GRAS status for components with FDA	✓							
Established collaboration with University of Liverpool (UK)		✓						
Completed product development plan		✓						
Patent Application filed				✓				
Commercial feasibility			✓					
Manufacturing – sourced suppliers		✓						
Proof of concept				✓				
Animal study (IBD)						F*		
Human observational study (IBS)						S*		
Partnering discussions								F*

* **F**inish; **S**tart

Source: Company

After pre-clinical safety of GaRP is confirmed in animal models, the company will look for a potential partner to market the product (Figure 1). Considering that Anatara has sufficient cash from its recently executed Zoetis deal, we believe the milestones are achievable.

There is significant market opportunity for GaRP in treatment of IBS/IBD

A decade ago it was estimated that one in four persons on prescription medication also take a dietary supplement for GI disorders[12]. A more recent estimate has suggested one in two[13]. With increasing education about dietary supplements and their more detailed evaluation, healthcare providers are working with patients to develop individualized programs that include dietary supplements for symptom management in GI disorders. This has led to a rise in adoption of dietary supplements, indicating a significant market potential for GaRP.

Prevalence numbers of IBS are attractive

Prevalence of IBS is quite high in US and EU; it is projected to increase in developing countries as they become 'westernized'

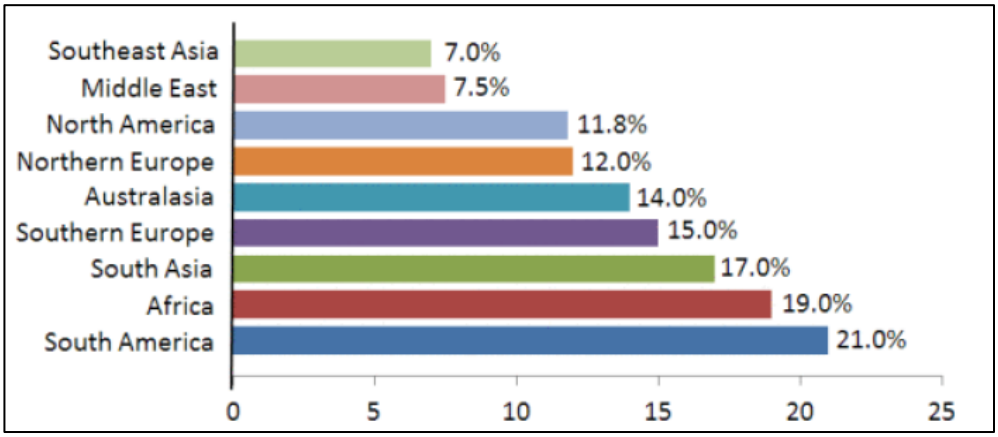
IBS is a functional disorder[14] characterized by abdominal pain, bloating, and alternating constipation and diarrhea. Though the syndrome is marked by a low level of inflammation (versus IBD), it still compromises the functioning of the gut. The market opportunity for GaRP in this segment is significant,

[12] Am Fam Physician. 2008 Jan 1;77(1):73-78; Arch Intern Med. 2006;166(18):1968-1974.
[13] World J Gastroenterol. 2014 Jan 14;20(2):346-62
[14] Functional disorders are conditions where there is an absence of structural or biochemical abnormalities on common diagnostic tests, which could explain symptoms.

considering the high worldwide annual prevalence rates of IBS – averaging ~11%[15] and typically in the range of 5–20%[16]. Geographically, the disease is prevalent in both developing and developed countries, with more recent studies indicating an increasing prevalence in newly developed and developing economies (i.e., Asian countries) as they become 'westernized'[17]. In North America, the prevalence rates stand at ~11.8% and in the EU, the corresponding figure ranges between 12% and 15% (Figure 2).

Moreover, according to the World Gastroenterology Organization (WGO), IBS with predominant diarrhea forms one-third of the total cases of IBS. Considering that GaRP is expected to be positioned to treat IBS patients with diarrhea (based on its anti-secretory properties), the market is quite lucrative.

Figure 2: Prevalence Rate of IBS



Source: Clin Gastroenterol Hepatol. 2012 Jul;10(7):712-721.e4

Further, recent evidence has confirmed the role of intestinal microbiota in predicting the severity of IBS[18]. Studies also suggest that the use of complementary and alternative medicines (CAM)[19] is highly prevalent in patients with IBS, with ~50% of patients using dietary supplements for symptom management[20]. In fact, diet or lifestyle modifications are often advocated as the first step in the management of IBS. Research indicates that supplements with the potential to be used for the management of IBS symptoms include probiotics, prebiotics[21], fiber supplements (e.g., psyllium)[22], herbal supplements (e.g., peppermint oil)[23], curcumin (turmeric), and vitamin supplements (e.g., vitamin D)[24]. According to Mordor Intelligence, the global market for dietary supplements is expected to grow at a 6.9% CAGR during 2017–2023 to reach >US$135bn. A major growth driver is the popularity of herbal and probiotic supplements. Some of the key global players that have already developed dietary supplements include Bio-Botanica, Bayer, BASF, Ricola, Herbalife, and Integrated BioPharma. With

[15] Clin Gastroenterol Hepatol. 2012 Jul;10(7):712-721.e4.
[16] World J Gastroenterol. 2014 Jan 14; 20(2): 346–362.
[17] IBS Global Impact Report 2016, published by Allergan.
[18] Gastroenterology. 2017 Jan;152(1):111-123.e8
[19] CAM consists of products that are not considered mainstream, or conventional, medicine. This can include herbal therapy or phytotherapy, dietary supplementation, probiotics, Chinese medicinal practices (e.g., herbal supplements or acupuncture), mindfulness, or other mind–body therapies.
[20] J Altern Complement Med. 2018 Sep 12.
[21] Curr Opin Clin Nutr Metab Care. 2011 Nov;14(6):581-7.
[22] Int J Mol Med. 2017 Sep;40(3):607-613.
[23] World J Gastroenterol. 2014 Jan 14; 20(2): 346–362.
[24] Williams CE, et al. Eur J Clin Nutr. 2018;doi:10.1038/s41430-017-0064-z.

GaRP's ability to restore the normal microbial function of the gut, the compound has a significant uptake potential in the dietary supplements market.

Expected growth opportunity in IBD space bodes well for GaRP

~50% IBS patients use dietary supplements for symptom management

IBD is an umbrella term used to describe all disorders that involve chronic inflammation of the digestive tract. The disease is characterized by symptoms such as abdominal pain, cramping, bloating, blood and mucus in stool, loss of appetite, and persistent diarrhea. There are two major types of IBD – ulcerative colitis, where the inflammation impacts the inner lining of the gut, and Crohn's disease, in which the whole wall of the gut is inflamed. Due to a high level of inflammation, both disorders present a significant market opportunity for GaRP.

More than 5 million people suffer from IBD worldwide[25]. We estimate that there are ~2.5 million patients in the EU and 1–1.3 million in the US[26]. In the US, roughly 40% of these people suffer from Crohn's disease and the remaining 60% have ulcerative colitis. Moreover, IBD has also emerged in newly industrialized countries in Asia, South America, and the Middle East, and is fast evolving into a global disease. Scientists project that the prevalence of IBD is expected to rise exponentially by 2025 due to cumulative addition of incident cases in a chronic disease that has a young age of onset and low mortality (Figure 3).

Figure 3: Prevalence of IBD

Source: Nat Rev Gastroenterol Hepatol. 2015 Dec;12(12):720-7

To manage the disease symptoms, people often turn to CAM as an adjunct to prescription medicines. Over the past few decades, the use of CAM has increased in popularity, particularly in North America and Europe,[27] and studies suggest that 30–50% of IBD patients use CAM for treatment[28]. Drivers for the increasing uptake of CAM include the perception that herbal remedies are natural, less toxic, or harmless; a lack of response to or undesirable side

[25] Crohn's and Colitis Australia.
[26] Nat Rev Gastroenterol Hepatol. 2015 Dec;12(12):720-7.
[27] Inflamm Bowel Dis. 2013;19(4):767-778
[28] Gastroenterology 2017: 152:415–429

30–50% of IBD patients use CAM to reduce symptoms

effects of conventional therapy; and the desire to improve quality of life (QoL). This indicates that GaRP has an opportunity to target nearly half of the total IBD population (i.e., an estimated 2.5 million patients worldwide), representing an attractive opportunity for Anatara. Moreover, considering the predictions related to the rise in global disease burden, this opportunity is expected to continue to grow over the next decade.

Currently, herbal and dietary supplements being used as an adjunct to prescription medicines for symptom management in IBD include curcumin, cannabis (medical marijuana), fish oil, probiotics/pre-biotics, vitamin D, and Chinese herbal medicine[29,30]. Mordor Intelligence predicts that the market for curcumin is expected to rise at a CAGR of ~12% over 2018–2023 and reach US$85m, driven by an increase in demand for curcumin food supplements. Meanwhile, MarketsandMarkets predicts that the probiotics market is expected to reach US$64bn by 2022, growing at a CAGR of 7% during 2017–2022.

The evidence indicates that the opportunity for GaRP to grab a share in the dietary supplements market for both IBD and IBS is quite high, and this trend is anticipated to continue to grow over the next 5–10 years.

Detach – Anatara's out-licensed product for animal health

Detach's characteristics make it a lucrative candidate for scour

Detach has a broad spectrum of anti-microbial activity that enables it to act against a wide array of pathogens including *E.Coli* and *V. cholera*[31].

Detach is known as an immune modulator: Detach has strong anti-inflammatory properties, although the exact mechanism by which it exerts anti-inflammatory effects is not yet fully understood[32]. Taking inflammation down reduces tissue damage to the intestinal wall, thereby reducing the potential for diarrhea[33].

Detach is stable at room temperature. This allows the product to be used in markets that lack cold chain pharmaceutical infrastructure.

Detach is a safe for consumption. Bromelain has long been granted GRAS status. Moreover, studies conducted by Anatara on pigs have shown that the drug is safe and well-tolerated at the recommended doses.

Detach benefits from concerns over traditional anti-microbials and antibiotics. In the wake of concerns over antimicrobial resistance (AMR), antibiotics have become very unpopular of late. For instance, Zinc oxide – known to be effective as an anti-microbial in pigs[34] – is banned in some countries, due to its issues pertaining to AMR and environmental implications as a heavy metal. Although copper sulfate – another compound with similar activity – is not banned, it is also considered to adversely impact the environment[35].

[29] Curr Pharm Des. 2016;22(2):180-8.
[30] Gastroenterology and Hepatology. 2018; 14(7).
[31] See Gut. 1996 Jan;38(1):28-32; Gastroenterology. 1997 Jul;113(1):175-84; J. Immunol, 1999.163:2568-2575 and Gastroenterology. 1997 Jul;113(1):175-84.
[32] Journal of Autoimmune disorders. 2017;3:52.
[33] Ann N Y Acad Sci. 2009 May;1165:285-93.
[34] Res Vet Sci. 1998 May-Jun;64(3):225-31.
[35] Springerplus. 2013; 2: 498.

Competition from alternatives is limited. Various oral vaccines as well as probiotics are available as alternatives, but these approaches are typically expensive. Moreover, a low protein diet or organic acids exert similar action but may also affect the quality of meat produced. Therefore, Detach appears to be a superior option.

Anatara has met key milestones for Detach

Detach's discovery dates back to 1980s. When Detach was launched in 1991 by Ciba-Geigy, it had gained a market share of ~40% in the market for pig health. Anatara was founded in 2010 in order to redevelop the drug with a new formulation. Before out-licensing Detach to Zoetis in May 2018, Anatara had made a significant progress with the drug's scientific development and achieved major regulatory milestones in key markets.

Scientific Development Milestones (FY2014–FY2017)

When Anatara Lifesciences went public on the ASX in October 2014[36] it was the third public company to have been involved in the development of bromelain as an anti-infective in animal health. At that time, the company's primary goal was to develop Detach as a non-antibiotic to aid control of scour in piglets.

During FY2014–FY2016, the company conducted field trials in commercial piggeries in Australia. The results were extremely promising, reducing piglet mortality by almost half. Moreover, a pivotal Target Animal Safety (TAS) study completed in September 2016 indicated that Detach is safe even when administered at higher doses and more frequently than recommended.

In FY2017, the company revealed that it had developed a proprietary dosing device for optimal delivery of Detach by pig farmers.

Regulatory/Commercial Milestones (FY2017–FY2018)

Anatara also already achieved certain commercial milestones in key global markets before and after Detach's out-licensing agreement with Zoetis was announced:

- **Australia**: In October 2018, Anatara received APVMA[37] approval of Detach for the treatment of scour in piglets; the approval was based on positive results from the drug's field trials and is expected to further aid Zoetis' commercialization efforts in Australia.
- **US**: In February 2018, Anatara received a 'complete letter' from the US FDA for the technical section of its Human Food Safety (HFS) submission. The letter confirms that the US FDA's Office of New Animal Drug Evaluation, Center for Veterinary Medicine, is satisfied with the human safety requirements for Detach and that the food products from animals treated using Detach are considered safe for human consumption. This decision is expected to catalyze the registration of Detach in one of the most important markets globally.
- **Europe**: Following an extensive review process, in June 2017, Anatara received a positive note on the MRL status of bromelain from the European Medicines Agency (EMA) confirming that the compound is non-toxic and can be safely used as a therapeutic in pigs. The status is a significant outcome as it confirms that Detach is safer vis-à-vis antibiotics.

Detach has already received APVMA approval

[36] After raising $7m at 50 cents per share.

[37] Refers to Australian Pesticides and Veterinary Medicines Authority (APVMA); the Australian Government statutory agency responsible for the management and regulation of all agricultural and veterinary chemical products in Australia.

The Zoetis global licensing deal

The licensing deal with Zoetis took over two years to finalize

In January 2016, Anatara entered into an exclusive option agreement with Zoetis, under which Zoetis gained exclusive rights to evaluate the potential applications of Detach for veterinary use in food production animals in all countries, except Australia and New Zealand. During the option period, Anatara received upfront and subsequent cash payments and the two companies agreed to evaluate Detach's potential in multiple livestock species in an aggressive research program.

Following the preliminary evaluation for more than one year, Zoetis agreed to exercise its option to negotiate for a commercial agreement and the two companies entered into negotiations for the worldwide development of Detach in August 2017. In May 2018, Zoetis gained an exclusive worldwide license (including Australia and New Zealand) of Detach.

The deal terms are beneficial for Anatara

Under the terms of the deal, Anatara would get a significant cash flow for future development of bromelain-based products, at least for the next few years. The terms include:

- A$2.5m upfront payment with A$2m credited against previously paid fees
- Milestone payments of up to A$6.3m, subject to first commercial sales and total annual sales exceeding a certain amount
- Royalties on product sales in the range 3–4%

Considering the size and scale of Zoetis, the potential reach of Detach is anticipated to be vast. Therefore, we believe that the deal will help significantly in keeping Anatara financially robust.

Anatara's deal with Zoetis is expected to keep the company well-funded over the next few years

Zoetis is a good partner for Anatara

After evaluating Detach for over 2 years for use as a non-antibiotic product in livestock, in May 2018, Zoetis signed an exclusive licensing agreement with Anatara for the worldwide development, manufacturing, distribution, and marketing of Detach for livestock animals and horses.

Zoetis is expected to be able to contribute more effectively to Detach's development and marketing

In our opinion, the deal would serve as a catalyst for the development of Detach considering that Zoetis is one of the largest animal health companies with 60+ years of experience and derives at least two-thirds of its US$5bn revenues from farm animal health products (therefore, Detach fits well in the portfolio). Moreover, Zoetis consistently spends 7–9% of revenue on R&D – an annual budget of US$350–400m. Based on these evidences, the agreement is expected to overcome Anatara's limitations on all 4 aspects of the deal:

- **Development**: Zoetis plans to develop Detach for use in a range of livestock species and horses. Such significant effort would have been outside of Anatara's capacity as a small company.
- **Manufacturing**: The company is backed by its wide manufacturing footprint, helping in bulk production of the drug during its development and launch.
- **Distribution**: Zoetis sells its products to 120+ countries. Such a huge network base is expected to facilitate the distribution of Detach to a wider audience.

– **Marketing**: Considering the difficulties associated with marketing animal products, Zoetis' unmatched expertise in the industry will certainly provide an edge over Anatara's experience as a relatively smaller firm.

Detach gets access to larger and more diverse markets while Anatara's cost burden reduces

We view the agreement as a major milestone for the company for three main reasons. First, it includes all livestock species and not only pigs (Anatara's initial focus area). Second, while Anatara was initially only focusing on the Australian market, the license is structured as a worldwide agreement. It, therefore, offers the potential to lead to multiple, larger markets for the product over time. Third, the deal reduces the burden on Anatara as it no longer has to bear any costs associated with the development and registration of Detach for other species and territories. Meanwhile, it continues to receive royalty on sales and milestone payments to fund its future R&D efforts. These characteristics make the agreement very attractive for Anatara with a potential to generate long-term shareholder value.

Opportunity for Detach's uptake in markets targeted by Zoetis is quite significant

Huge opportunity in livestock on the back of increasing meat consumption

While pork consumption may decline marginally by 2030, it is still expected to remain at 33% at least of total meat consumption

In recent years, global meat production and consumption has increased rapidly and is expected to continue to rise over the next few decades. The Food and Agriculture Organization (FAO) estimates that between 1997/99 and 2030, annual meat consumption in developing countries is projected to increase from 25.5 to 37 kg per person, and 88 to 100 kg in industrial countries. FAO numbers also suggest that globally, livestock production is expected to increase at an annual growth rate of 1.5% with the number in developing countries expected to grow at an annual rate of 2.1%. Meanwhile, the global antibiotics and antimicrobials market is expected to exceed US$4.7bn in 2022. Considering the recent concerns of policy makers about the consequences from the long and growing use of antibiotics in livestock production, there is an urgent need for alternatives to antibiotics. Thus, natural products, such as Detach, have a significant uptake potential as an alternative for antimicrobials.

Pigs represent a lucrative opportunity as an initial target segment

The opportunity for Detach in pig production, as an initial sector, is attractive because pork is currently the most consumed meat globally. Every year humans eat on an average ~41 kg of meat, ~37% of which is pork, followed by poultry at 33%, beef at 24% and lamb/mutton at 5%. According to FAO, per capita pork consumption is expected to decline marginally in favor of more expensive meat sources by 2030, but pork will remain at least 33% of total meat consumption during this timeframe. Moreover, according to FAO estimates, global pork production – currently 110 million tones p.a. – will match the rise of global population growth, which is around 1% p.a.[38] Also, ~1.6 billion piglets are weaned each year, 20% of which die due to health

[38] Source: Food and Agriculture Organization, *World agriculture: towards 2015/2030*, 2003.

issues. This indicates a significant unmet need for options to increase production to meet the growing pork demand – a gap that Detach claims to be potentially able to fill.

A study published in the trade publication *Milne's Pork Journal*[39] in 1991 concluded that the original formulation of Detach had a very high revenue potential and that at least A$5 per pig could be realized from the use of Detach. While this is an old study, in our opinion, this is an indication that favorable economics can be realized for Anatara's current Detach formulation. China, the largest pork-producing country, accounts for half of the total global pork production (Figure 4), while developing countries including Brazil, Russia, Vietnam, the Philippines, and Mexico contribute another 10%. This proves that the economics of Detach are compelling for a significant portion of world's pig producers.

A 1991 study stated that at least A$5 per pig could be realized from the use of original Detach formulation

Figure 4: Top 10 Pork-Producing Countries

Top 10 Pork-Producing Countries			
		Thousand Metric Tons	
		2016	2017
1	China	52,990	53,400
2	European Union	23,866	23,675
3	United States	11,320	11,610
4	Brazil	3,700	3,725
5	Russia	2,870	2,960
6	Vietnam	2,701	2,741
7	Canada	1,914	1,970
8	Philippines	1,540	1,563
9	Japan	1,279	1,282
10	Korea, South	1,266	1,280
	Others	6,691	6,722

Source: USDA Foreign Agricultural Service (updated as on May 5, 2018)

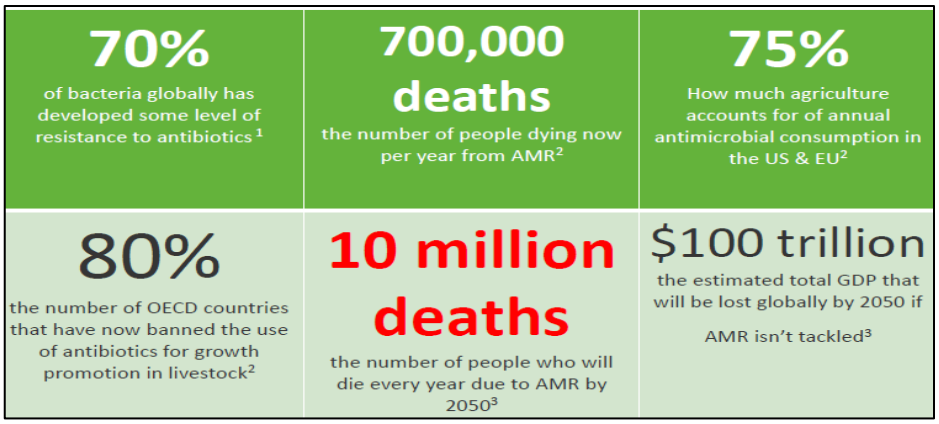
Market opportunity in horses comes from complexity of their GI tract

According to IBIS World, during 2013–2018, horse and other equine production in the US has grown to reach US$2bn in 2018[40]. The demand for horses is expected to be continued to be driven by strong millennial participation in recreational equine activities. To cater to this demand, there is a need for products that can at least sustain production levels. To add to this, the digestive tract of horses is complex, sensitive to the environment, and prone to complications. Also, it is often abused with overuse of antibiotics, nonsteroidal anti-inflammatories, de-wormers, and many other drugs. Furthermore, the population of microbiota varies widely in horses,

[39] Milne's Pork Journal 1991:13;32-34.
[40] Source: *Horse & Other Equine Production Industry in the US;* IBIS World, Oct 2018.

even among those kept on similar feeding programs. Therefore, there is a compelling need for natural products that can restore gut microbiota in horses – indicating a significant uptake potential of Detach.

Figure 5: Antimicrobial resistance in numbers



Sources: AMP Capital Insights Paper, 2017, "Is factory farming making us sick?"; OECD Antimicrobial Policy Insights Paper; Review of Antimicrobial Resistance, 2016 (amr-review.org), Final Report and Recommendations

Antimicrobial resistance is contributed by antibiotic use in production animals

Products that reduce anti-microbial resistance in the food chain are important

Anti-microbial resistance in the food chain is a cause of concern

Historically, antibiotics have played an important role in reducing mortality from infectious diseases, ever since Florey et. al. helped bring the first one, Penicillin, to market in the 1940s[41]. However, bacteria can become resistant to antibiotics when overused. This is driven by the natural mutations that occur in bacteria over time[42]. Antibiotic overuse speeds this process up by applying selective pressure for the survival of resistant strains.

Over 10 million people are expected to die every year due to AMR by 2050

For the past few years, antibiotic resistance is on the rise and has been a concern for policy makers. According to the World Health Organization, ~400,000 patients present with an antibiotic-resistant strain, resulting in ~25,000 deaths in the EU[43]. The comparable figures for the US are 2 million infections and 23,000 deaths[44]. By 2050, 10 million people are expected to die annually due to AMR (Figure 5).

Traditionally antibiotic resistant bacteria, such as Methicillin-Resistant *Staphylococcus Aureus* (MRSA) and multidrug resistant *Mycobacterium tuberculosis*, have been generated by antibiotic use in man. However growing evidence suggests that use of antibiotics in production animals has contributed to the antibiotic resistance problem[45]. While this evidence is not

[41] The Australian Howard Florey (1898–1968) won the Nobel Prize in Physiology or Medicine in 1945 alongside Sir Alexander Fleming (1881–1955) and Sir Ernst Chain (1906–1979) for the discovery of penicillin.
[42] Through either: (1) enzymatic degradation of antibacterial drugs, which is what generally happens with bacteria resistant to penicillins and cephalosporins; (2) alteration of bacterial proteins that are antimicrobial targets (which is what causes methicillin resistance); and (3) changes in membrane permeability to antibiotics.
[43] Nat Rev Microbiol. 2011 Nov 2;9(12):894-6.
[44] Source: CDC.
[45] Nutr Res Rev. 2000 Dec;13(2):279-99 and Int J Antimicrob Agents. 2000 Nov;16 Suppl 1:S19-24.

totally definitive[46], it is supported by the fact that most antibiotics are used in animals – in the US, production animals consume approximately four-fifths of all antibiotics consumed[47], while humans only account for the remaining 20%. Thus, increasing focus is being laid on antimicrobial resistance arising from antibiotic use in production animals.

What is being done to overcome the problem?

For the last few decades, public concern over the issue is gradually pushing down the use of antibiotics in production animals. In 1990s, the trend was widespread in Europe[48] and by 2007 it became apparent in the US as well when Perdue – one of the largest major chicken producers in the US – eliminated antibiotic use for growth promotion. A 2012 survey from Consumer Reports showed that 60% of respondents in the US would be willing to pay more for meat raised without antibiotics[49]. Soon, many Quick Service Restaurant (QSR) chains moved to deal with these concerns. For instance, in February 2014, Chick-fil-A, the US chicken restaurant chain with >2,000 stores, publicly committed to antibiotic-free chicken[50]. In March 2015, McDonald's, one of the biggest QSR operator globally with >37,000 restaurants, announced that it would phase out all meat sources that contained antibiotics. [51] Many competitors have followed suit, most notably Subway (October 2015[52]), In-N-Out Burger (March 2016[53]), Taco Bell (April 2016[54]), and Burger King (December 2016[55]). In June 2018 Pizza Hut committed to serve antibiotic-free chicken by 2022[56].

Meanwhile, public policy makers have also started to become concerned and have created action plans to overcome the issue of antimicrobial resistance. For instance, the EU banned antibiotic growth promotants in animal feed in 2006 and announced an 'Action Plan' designed to counter antimicrobial resistance in 2011. The US Congress, in 2012, passed the GAIN Act[57] to encourage the development of new products that would fight antimicrobial resistance. In 2016, the US FDA issued new rules that limit antibiotic use in farm animals generally, not just one particular type of livestock[58]. In June 2014, a Ministerial Conference on Antibiotic Resistance held in The Hague addressed, among other issues, the need for reduced antimicrobial use in production animals. Following this, in May 2015, the WHO adopted a global action plan on antimicrobial resistance to improve awareness and knowledge about related issues[59]. In September 2016, various Heads of State and Governments met at the UN Headquarters for a General Assembly on Antimicrobial Resistance and agreed that resistance to antibiotics is 'the greatest and most urgent global risk'[60].

[46] Foodborne Pathog Dis. 2007 Summer;4(2):115-33.
[47] Proc Natl Acad Sci U S A. 2015 May 5;112(18):5649-54. Epub 2015 Mar 19.
[48] Environ Health Perspect. 2014 Jun;122(6):A160-5.
[49] Source: *Consumer Reports*, Meat on Drugs, June 2012.
[50] See *Chick-fil-A commits to stop sales of poultry raised with antibiotics* by Stephanie Strom, *New York Times*, 11 February 2014.
[51] See the McDonalds policy document headlined *'McDonald's Global Vision for Antimicrobial Stewardship in Food Animals'* at mcdonalds.com.
[52] See the Subway press release headlined '*Subway Restaurants Elevates Current Antibiotic-Free Policy*' and dated 20 October 2015.
[53] See *In-N-Out vows to veer away from beef raised with antibiotics* by Bradley Zint, *LA Times*, 4 March 2016.
[54] Source: Statement Regarding Antibiotics, 18 April 2016 at tacobell.com.
[55] See *Burger King announces antibiotic-free chicken for 2017,* Fox News, 30 December 2016.
[56] See *Pizza Hut makes plans to use antibiotic-free chicken by 2022*, Meat+Poultry, 19 June 2018.
[57] Short for 'Generating Antibiotics Incentives Now', GAIN provides new 'qualifying infectious disease products' or QIDPs with an extra five years' US market exclusivity on top of whatever exclusivity they would otherwise have been granted.
[58] See Will new FDA rules curb the rise of antibiotic-resistant superbugs?, *The Guardian,* 8 January 2017
[59] Source: World Health Organization Press Release dated May 2015 *Global Action Plan on Antimicrobial Resistance.*
[60] Source: UN document headlined '*Draft political declaration of the high-level meeting of the General Assembly on antimicrobial resistance*' and dated 21 September 2016.

Valuing Antara

We value Anatara at $1.34 per share base case and $3.61 optimistic case using a probability-weighted DCF valuation approach.

Figure 6: Our valuation of Anatara

	Base	Optim.
Detach (A$m)	61.2	163.1
GaRP (A$m)	5.5	19.0
Value of tax losses	3.2	3.2
Underlying R&D cost	-9.6	-9.6
Cash now (A$m)	6.0	6.0
Cash from options and cash to be raised (A$	2.1	2.1
Total value (A$m)	68.4	183.8
Total diluted shares (million)	51.0	51.0
Value per share	$1.34	$3.61
Valuation midpoint	$2.47	
Share price now (A$ per share)	$0.360	
Upside to midpoint	586.9%	

Source: Pitt Street Research

General assumptions

Discount rate. We used a WACC of ~15%, appropriate in our view for a 'Speculative' risk rating[61];

Probability of success. For Detach we assumed no development or regulatory risk in terms of the product's ability to make it through field trials and receiving the requisite marketing approvals. Detach now primarily has commercial rather than development risk. With GaRP we assumed, for conservatism's sake, a 20% probability weighting to reflect the historic failure rate of therapeutics that have reached Phase 2.

Time horizon. We used a 14-year time horizon in our DCFs followed by a terminal value;

Currency. We assume the AUD/USD exchange converges on 0.7 over a three-year period from now.

Capital. We assume no further capital needs to be raised, with Anatara in a position to fund itself from Detach-related revenues from FY18.

Valuing GaRP

[61] 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 (2.7%) 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 Anatara to reflect the skepticism with which the market greeted the Zoetis deal of May 2018.

The challenge in valuing a product like GaRP is that licensing deals for functional foods tend to be infrequent, with shareholder value being built through developers launching their own product and then selling the brand or the company at a later stage to a large player in functional foods. We believe that this will change over time, as the functional food and pharmaceutical sectors converge[62]. Consequently, our thinking on valuation for GaRP has been guided more by pharma in-licensing. Given the lack of powerful Rx products in IBS and IBD, we think this is a reasonable approach.

We assume:

- Anatara can license GaRP to a prospective pharma or nutritionals partner in FY21 (optimistic case) or FY22 (base case);
- Global product launch beginning in FY24 (optimistic case) or FY25 (base case);
- Upfront payments post the licensing agreement of US$5-10m[63];
- Milestone payments as products are developed of US$20-40m. While we have not been able to identify benchmarks for milestones in functional food transactions, US$20-40m is way below those available in the typical for pharma licensing deal[64];
- Peak sales globally of ~US$300m (base case) to US$600m (optimistic case)[65].
- A royalty to Anatara of 4% (base case) to 8% (optimistic case)[66].

Valuing Detach

- First commercial launch outside Australia in FY20 (optimistic case) or FY21 (base case.
- Peak sales globally of ~US$900m (base case) to US$1700m (optimistic case).

Re-rating Anatara

We see a number of factors helping to re-rate Anatara towards our valuation range:

- Registration of Detach in key markets, such as the US and the EU;
- Positive results from efficacy and proof-of-concept studies of GaRP in IBD/IBS;
- Partnering or collaboration events related to GaRP.

Anatara's management team has significant experience in human health

Since 2016, Anatara's management has undergone significant changes. The new management team's experience aligns well with Anatara's focus areas,

[62] For background here consider the KPMG report from 2015 headlined *'Nutraceuticals: The future of intelligent food'*.
[63] When ChromaDex Corp. (Nasdaq: CDXC) licensed its Tru Niagen NAD supplement to Nestlé Health Science a US$4m upfront was disclosed.
[64] Consider, for example, the Protagonist / Janssen deal of 2017, where Protagonist Therapeutics (Nasdaq: PTGX) licensing an IBD drug candidate then in pre-clinical to Janssen for US$50m upfront payments and US$940m in milestones.
[65] We believe that a prescription drug targeting the same markets as GaRP could have sales of US$1.5-3bn based on the size of the patient population – for background consider Big Need in *IBD: Drugs to Slow Progression* by Gail Dutton, Genetic Engineering News, 1 August 2013. We estimate the functional food market to be around one fifth the size of the prescription drug market globally.
[66] That this is reasonable is suggested by the Ganeden/Schiff Nutrition deal of 2011 (3-7% for probiotics brands - source: Schiff Nutrition 10K filing for 2012).

as it positions itself for entry into new market segments and geographies to create long-term shareholder value.

Steven Lydeamore (CEO with effect from December 3, 2018) was appointed by Anatara on November 14, 2018. He replaced Dr. Tracie Ramsdale, who had been serving as interim CEO since May 2018 after Dr. Mel Bridges (the then acting CEO) announced his retirement. Steven has 26 years of international pharma experience and possesses a deep understanding of the human health space. He started his career in 1992 and held various finance roles in F.H. Faulding & Co.[67] (in Australia) over 10 years, followed by four years in the US at Mayne Pharma. Thereafter, he worked for more than a decade at Apotex – a Canada-based pharma company – and rose through the ranks to become President of its Apobiologix division. Before joining Anatara, he worked for Bionomics – a clinical-stage biopharma company – as the CFO for close to a year. Steven brings along rich experience in the pharma industry to sail Anatara through development of its new market strategy in human health.

Anatara's management has undergone significant changes in the past two years

Dr. Tracey Brown (Chief Development Officer) joined Anatara in September 2016, and is responsible for directing and managing the human product development program. Brown started her career in academic and commercial research institutes, and developed products related to the treatment of cancer, inflammation, and anti-aging. For the past 20 years, she has led product development teams and has a deep understanding of requirements for the identification and evaluation of commercialization assets.

Dr. Michael West (COO) started working for Anatara in July 2016. West has 28 years of development, formulation and scale-up manufacturing experience starting as postdoctoral scientist at SmithKline Beecham in the US for 2 years prior to becoming postdoctoral fellow at Centre for Drug Design and Development at the University of Queensland for 4 years. He worked at the Brisbane-based drug developer Alchemia from the late 1990s to 2015. He is a qualified Patent & Trade Marks Attorney specializing in technology transfer and IP management, which will help Anatara develop products for human health.

The company's **board** is also experienced and possesses the skills required for building a successful human health company.

- **Sue MacLeman**, currently acting Board Chair, has >30 years of experience and has held senior executive roles at ASX- and Nasdaq-listed pharma and biotech companies.
- **Dr. Tracie Ramsdale**, Board Director, has >30 years' experience in drug development and has held senior executive roles and board roles at ASX listed companies.
- **Dr. Jane Ryan**, Board Director, has >30 years of experience in fundraising campaigns and licensing initiatives for pharma and biotech companies.
- **Dr. David Brookes**, Board Director, has >20 years of experience in health and biotechnology industries having held board roles at ASX listed health and biotechnology companies and presently maintaining roles as a clinician and biotechnology industry consultant.
- **Stephen Denaro**, Company Secretary, has extensive experience in M&A, business valuation, accountancy services, and income tax compliance.

In October 2018, Anatara formed a Product Development Advisory Board with five key external experts – **Dr. Rebecca Burgell, Dr. Jakob Begun, Prof. Barry Campbell, Associate Prof. Simon Keely, and Prof. Peter Gibson** (who will

[67] An Australian pharma company acquired by Mayne Group in October 2001

serve as Chairman). The newly appointed advisory board will work closely with the management team and Anatara's board to advance the human gastrointestinal health program.

Appendix I – Glossary

Adhesins – Proteins used by bacteria to adhere to the gut wall. Adhesins are often in the form of fimbriae, i.e., appendages on the bacterium (fimbria is the Latin word for fringe).

Antibiotic – Medicines that inhibit growth of bacteria and fight bacterial infections.

Antibiotic Resistance – The ability of bacteria to avoid being killed by antibiotics.

Antimicrobial – An agent that kills microorganisms or stops their growth.

APVMA – Short for the 'Australian Pesticides and Veterinary Medicines Authority', the government agency overseeing drugs for veterinary use in Australia.

Bromelain – A mixture of enzymes found in pineapples that have proteolytic properties. Anatara's Detach product is a modified-release formulation of bromelain.

Cyclic AMP, Cyclic GMP – Two 'secondary messengers' that help send signals in cells. They are cyclic in terms of their shape. AMP is adenosine monophosphate while GMP is guanosine monophosphate.

Dietary Supplement – A manufactured product intended to supplement the diet when taken orally as a pill, capsule, tablet, or liquid.

Drench – A dose of medicine administered to an animal.

Enterocyte – The most abundant epithelial cell lineage in both small and large intestines that plays an active role in defending epithelial surfaces. These cells secrete a variety of antimicrobial proteins that directly attack or kill bacteria.

Enterotoxigenic E. coli (ETEC) – The gut bacterium, Escherichia coli, which produces toxins that stimulate the lining of the intestines, causing excessive fluid secretion and, thus, diarrhea.

Enterotoxin – A protein exotoxin produced and secreted by microorganisms that targets the intestine.

Enzyme – A protein that helps speed-up biochemical reactions in the body. Enzymes generally have the suffix 'ase' in their name.

Excipient – An inert substance used to prepare a drug for administration rather than being an active part of the drug itself.

Feed Conversion Ratio – A measure of the efficiency with which a production animal converts food into protein. It is measured by kilograms of feed required to produce 1 kg of meat, where the meat is measured either as dressed weight or live weight.

Field Trial – A research method used to estimate the effect of an intervention on a particular outcome of interest.

GRAS – Short for 'Generally Regarded as Safe', a product with a long history of use and therefore with a well-known safety record.

Hemostasis – A complex physiological process, usually activated upon injury to blood vessels, that stops bleeding and keeps blood within a damaged blood vessel.

Inflammatory Bowel Disease (IBD) – Inflammation in the gut, where the inflammation affects either just in the inner lining of the gut (ulcerative colitis) or the whole wall of the gut (Crohn's disease).

Irritable Bowel Syndrome (IBS) – A functional disorder in which the bowel, while not inflamed or ulcerated, still doesn't work as it should. Symptoms of IBS include pain, bloating, gas, mucus in the stool, diarrhea, and constipation.

Microbiota/Microbiome – Microbiota refers to a community of microorganisms in a specific niche, such as the human gut. The microbiome comprises all of the genetic material within a microbiota.

Mortality – The death rate, measures the number of deaths in a particular population per unit time.

Natural Product – A drug that occurs in an unmodified form in nature. For example, Penicillin is a natural product derived from the mould Penicillium chrysogeum. Bromelain is a natural product.

Phthalates – Chemicals commonly used as 'plasticizers', increasing the flexibility of plastics so they are harder to break. Phthalates are often used as excipients in orally available medicines.

Prebiotics – Prebiotics are non-digestible food ingredients that probiotics can feed on. These products are used to increase populations of healthy bacteria in the gut, aid digestion, and enhance the production of valuable vitamins.

Probiotics – Include live beneficial bacteria that are naturally created through fermentation in foods such as yogurt, sauerkraut, miso soup and kimchi.

Proteases – Enzymes that hydrolyze the peptide bond between amino acid residues in a polypeptide chain.

Proteolytic – Capable of breaking down proteins.

Scour – Another name for diarrhea in livestock.

Sucker – A piglet before it has been weaned, which generally happens at or around day 21.

Target Animal Safety Study – The study that aims to establish that a drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labelling.

Weaner – A piglet that has been weaned. Historically piglets become weaners between three and five weeks of age. For study purposes, Anatara has used day 21 as the day a piglet becomes a weaner.

Appendix II - Detach field studies in pigs

Figure 7: Summary of Detach (old formulation) field trials conducted during 1988–1991

Detach™ trial summary	Suckers	Weaners
Number of trials	11	8
Number of piglets	4,752	2,880
Improved average daily weight gain	12.7%	8.6%
Reduction in mortality	42.4%	41%
Reduction in antibiotic use	67.4%	31%
$ Benefit/100 head*	$526	$299

Source: Lindsay, L. 1991. Auspig model indicates new scours treatment could boost returns by $5.18 a pig. Milne's Pork Journal. 13:32-33

Historic background

In field trials, Detach has shown reduction of scour in pigs. Scour is a major disease that can lead to a decrease in the number (due to mortality) and weight of production animals – including pigs – and is caused by pathogenic *E. coli* and other bacteria[68]. As a prophylactic measure, farmers often feed antibiotics daily to their animals. By contrast, Detach has been shown to reduce scour with only two oral doses[69] – a 2 ml 'drench' as a sucker (when the piglet is between two to five days old) – and a 4 ml drench as a weaner (i.e., after the piglet has been weaned from its mother, around day 21).

During 1988–2001, Cortecs conducted multiple field studies on the old formulation of Detach (Figure 7). Anatara, upon acquiring this technology, analyzed 19 field studies in both suckers and weaners that covered >7,500 animals and found that Detach, on average, improved daily weight gain by 11%, reduced mortality by over 40%, and cut antibiotic use by half[70].

Anatara's field studies, 2012–2016

Detach's field trials show significant reduction of scour incidence and improvement in FCR

2012 EU study in weaners: This study, conducted in commercial pig farms in the EU, demonstrated that the new formulation of Detach reduces the incidence of post-weaning scour in treated pigs by 40% and lowers antibiotic use by 55%. In each case, these results had statistical significance ($p<0.05$). Detach also improved average daily weight gain by 22%.

Historically, a key metric in pig farming has been the 'feed conversion ratio (FCR)', which measures the kilograms of feed required to produce one

[68] J Vet Intern Med. 2004 Jan-Feb;18(1):8-17.
[69] Delivered by mouth using a measured dosing applicator.
[70] Source: Lyndsey, 1991. Milnes Pork Journal article on Detach and Anatara Lifesciences prospectus dated 4 September 2014, page 21.

kilogram of pig meat. In the EU studies, this featured as an important metric. In one trial on 267 weaner pigs in France, Detach improved FCR by 33% when compared with piglets treated with an antibiotic (colistin). In another trial on 216 piglets in Spain[71], Detach improved FCR by 4.2% compared with piglets administered with an antimicrobial (zinc oxide). Both trials suggested that Detach provides superior FCR benefits when compared with the currently used products for scour (Figure 8).

Figure 8: Detach (new formulation) field trials conducted in 2012

Field Study	Comparisons	Improvement in FCR (%)
Spain	Detach™ vs ZnO	4.2%
	Detach™ vs No treatment	2.7%
France	Detach™ vs Colistin	33%
	Detach™ vs No treatment	7%

Source: Anatara Lifesciences prospectus dated 4 September 2014, page 21

2015 study in suckers and weaners: After completing trials of Detach's new formulation in the EU, Anatara conducted additional field studies in Australia to facilitate its registration in the country. The trials aimed to investigate the ability of Detach to reduce the incidence, severity, and duration of scour compared to placebos. The company completed two field trials in 2015 – one in suckers and the other in weaners[72]. The first study in suckers[73] (February 2015) was a randomized, blinded, and controlled study that was conducted on a commercial pig farm in Northern Victoria that had a problem with pre-weaning scour despite the use of prophylactic antibiotics[74] and sow vaccines. In 233 treated suckers versus 229 untreated controls, Detach administered two days after birth[75] had shown a reduction in piglet mortality in the treated pigs to 8% compared to 16% for the untreated controls. This was statistically significant ($p<0.02$), while treated pigs also registered an average daily weight gain to weaning (at day 21) of the surviving pigs by 5.2%.

The study in weaners (September 2015) evaluated Detach on a commercial pig farm in southeast Queensland[76]. In 280 treated weaners who were dosed at day 21 versus 280 untreated controls, Detach reduced the frequency of scour by 41%, while the severity of scour[77] came down by 45% over the next 28 days. This outcome was statistically significant in each case ($p<0.02$). The treated pigs, however, experienced only a 1% increase in average daily weight gain. Unlike the study in suckers, the piglets in this study had no antibiotic use.

Safety studies show that Detach is safe even at higher dosage than recommended

Target Animal Safety Study: In September 2016, Anatara completed a pivotal target animal safety (TAS) study of Detach in 40 piglets (2 days old). The study showed that Detach is safe when administered orally at the recommended dose rate (2ml) and even at 3x (6ml) and 5x (10ml) of the recommended dose.

[71] Anatara code name ANR 12-001.
[72] Another study had been announced in June 2016 – in suckers to expand the proposed label that would give the pig farmer the option to either dose once or twice. However, this study was terminated by Anatara on 23 June 2016 when various 'extreme conditions' including power and water shortages caused the removal of substantial numbers of pigs from the trial site
[73] Trial code ANR 14-001
[74] Such as neomycin, trimethoprim and sulfadiazine.
[75] Since scouring tends to show up in suckers at day 3 or 4.
[76] Trial code ANR 15-001
[77] Where each scour occurrence was rated 1 or 2, the more severe being 2.

The results of all these studies ultimately resulted in the registration of Detach in October 2018 when the APVMA approved the product for use in Australia. Since worldwide rights to the product's development are now out-licensed to Zoetis, the approval is expected to aid the development and registration of Detach in other key geographies globally.

Appendix III – Capital Structure

		% of fully diluted	Note
Ordinary shares, ASX Code ANR (million)	49.4	96.9%	
Unlisted options (million)	1.6	3.1%	Exercise price 131 cents, average expiry date 25-Oct-2020
Fully diluted shares	51.0		

Current market cap:	A$17.8 million (US$12.6 million)
Current share price	$0.360
Twelve month range	$0.36 - $1.70
Average turnover per day (last three months)	20,800 shares

Appendix IV – IP Position

Anatara's IP derives from the following applications:

Enzymatic fractions with anti-inflammatory activity, WO/2017/031299, priority date August 20, 2015, invented by Tracey Mynott and Christian Engwerda.

- This patent application pertains to a method of refining crude bromelain extract by ion-exchange chromatography to improve anti-inflammatory activity. The chromatography is performed on a sepharose column and uses an acetate-based buffer for washing and elution.

Anti-diarrhea formulation which avoids antimicrobial resistance, WO/2016/032944, priority date August 25, 2014, invented by Tracey Mynott and John Walsh.

- This patent application pertains to an orally administrable, bromelain-based medicinal composition (for treating diarrhea), which contains sodium

carboxymethyl cellulose as a gelling agent, lecithin oil as an emulsifier, and EDTA and anhydrous citric acid as chelating agents. Unlike conventional antibiotics – which can lead to the development of resistant pathogenic strains – the composition does not destroy pathogenic cells, but prevents their adhesion on intestinal cells.

Appendix V – Papers Relevant to Anatara

Mynott et. al., 1991. *Efficacy of enteric-coated protease in preventing attachment of enterotoxigenic Escherichia coli and diarrheal disease in the RITARD model.* Infect Immun. 1991 Oct;59(10):3708-14 (full text available for free online).

- This paper shows that bromelain when administered to rabbits prior to infection with ETEC, reduced diarrhea and diarrhea-induced death in six of seven treated rabbits. By contrast seven of eight rabbits not protected by protease treatment died or developed severe diarrhea. The bromelain reduced the levels of bacteria by 2,000-fold ($p< 0.001$).

Mynott et. al., 1996. *Oral administration of protease inhibits enterotoxigenic Escherichia coli receptor activity in piglet small intestine.* Gut. 1996 Jan;38(1):28-32 (full text available for free online).

- This paper shows that bromelain has the potential to modulate adhesin ETEC attachment sites in the guts of piglets, thereby preventing attachment. Oral administration of the bromelain reduced ETEC attachment via an adhesin called K88 in a dose-dependent manner ($p < 0.05$).

Mynott et. al., 1997. *Bromelain prevents secretion caused by Vibrio cholerae and Escherichia coli enterotoxins in rabbit ileum in vitro.* Gastroenterology. 1997 Jul;113(1):175-84.

- This paper shows that bromelain pre-treatment could inhibit the secretion of bacterial toxins. This paper established the effectiveness of bromelain not just on ETEC but also on cholera toxins.

Chandler and Mynott, 1998. *Bromelain protects piglets from diarrhea caused by oral challenge with K88 positive enterotoxigenic Escherichia coli.* Gut. 1998 Aug;43(2):196-202 (full text available for free online).

- This paper reports a field test of bromelain in piglets, in which weaned piglets were fed bromelain and then challenged with K88+ ETEC. Bromelain reduced the incidence of diarrhea and the treated pigs experienced a statistically significant increase in weight gain compared with untreated pigs. However, the effect of bromelain treatment was only temporary, with enterocytes regenerating within 30 hours of treatment.

Mynott et. al., 1999. *Bromelain, from pineapple stems, proteolytically blocks activation of extracellular regulated kinase-2 in T cells.* J Immunol. 1999 Sep 1;163(5):2568-75 (full text available for free online).

- This paper demonstrates that bromelain inhibits T cell activation by blocking a kinase called ERK-2.

Engwerda et. al., 2001. *Bromelain activates murine macrophages and natural killer cells in vitro.* Cell Immunol. 2001 May 25;210(1):5-10.

- This paper shows that bromelain amplifies the performance of macrophages and the natural killer cells – the two key elements of the innate immune system.

Engwerda et. al., 2001. *Bromelain modulates T cell and B cell immune responses in vitro and in vivo.* Cell Immunol. 2001 May 25;210(1):66-75.

- This paper shows that bromelain has an indirect stimulatory action on T cells and increases the costimulatory activity of accessory cell populations.

Mynott et. al., 2002. *Proteolytic inhibition of Salmonella enterica serovar typhimurium-induced activation of the mitogen-activated protein kinases ERK and JNK in cultured human intestinal cells.* Infect Immun. 2002 Jan;70(1):86-95 (full text available for free online).

- This paper demonstrates that bromelain inhibits MAP kinase signaling pathways. These pathways are used by Salmonella and similar bacteria in inducing intestinal barrier dysfunction.

Hale et. al., 2004. *Proteolytic activity and immunogenicity of oral bromelain within the gastrointestinal tract of mice*. Int Immunopharmacol. 2004 Feb;4(2):255-64.

- This paper demonstrates that bromelain enzymes can remain intact and proteolytically active within the murine gastrointestinal tract.

Hale et. al., 2005. *Treatment with oral bromelain decreases colonic inflammation in the IL-10-deficient murine model of inflammatory bowel disease.* Clin Immunol. 2005 Aug;116(2):135-42.

- This paper shows that oral bromelain decreases the incidence and severity of spontaneous colitis in IL-10-/- mice. It also decreases the clinical and histologic severity of colonic inflammation in mice with established colitis.

Onken et. al., 2008. *Bromelain treatment decreases secretion of pro-inflammatory cytokines and chemokines by colon biopsies in vitro.* Clin Immunol. 2008 Mar;126(3):345-52 (full text available for free online).

- This paper shows how bromelain can be a novel treatment for IBD. Bromelain treatment *in vitro* decreases secretion of G-CSF, granulocyte-macrophage colony-stimulating factor (GM-CSF), IFN-gamma, CCL4/macrophage inhibitory protein (MIP)-1beta, and TNF by inflamed tissue in IBD.

Muller et. al., 2012. *Placebo-controlled randomized clinical trial on the immunomodulating activities of low- and high-dose bromelain after oral administration - new evidence on the anti-inflammatory mode of action of bromelain.* Phytother Res. 2013 Feb;27(2):199-204.

- This paper provides evidence that bromelain modulates the cellular responses of lymphocyte after oral use.

Nguyen et. al., 2018. *Influence of low-protein diets and protease and bromelain supplementation on growth performance, nutrient digestibility, blood urine nitrogen, creatinine, and faecal noxious gas in growing–finishing pigs.* Canadian Journal of Animal Science, 2018, 98(3): 488-497.

- This paper shows that supplementation of low-protein diet with protease and bromelain enhances growth performance, nutrient digestibility, and reduces NH3 and H2S in growing–finishing pigs.

Appendix VI – Companies to Watch

Company	Location	Code	Market cap (USDm)	Web
Kindred Biosciences	San Francisco, Ca.	Nasdaq: KIN	415	www.kindredbio.com
ECO Animal Health Group	New Malden, UK	LSE: EAH	405	www.ecoanimalhealthgroupplc.co
Paratek Pharmaceuticals	Boston, Ma.	Nasdaq: PRTK	231	www.paratekpharma.com
ChromaDex	Irvine, Ca.	OTCBB: CDXC	215	www.chromadex.com
Aratana Therapeutics	Kansas City, Ks	Nasdaq: PETX	213	www.aratana.com
CorMedix	Bridgewater, NJ	NYSE MKT: CRM	196	www.cormedix.com
Protagonist Therapeutics	Milpitas, Ca.	Nasdaq: PTGX	173	www.protagonist-inc.com
Oasmia Pharmaceutical	Uppsala, Sweden	Nasdaq OMX Stc	166	www.oasmia.com
Biosearch	Grenada, Spain	BME: BIO	102	www.biosearchlife.es
Tetraphase Pharmaceuticals	Watertown, Ma.	Nasdaq: TTPH	61	www.tphase.com
AB-Biotics	Barcelona, Spain	BME: ABB	60	www.ab-biotics.com
Achaogen	South San Francisco, Ca.	Nasdaq: AKAO	40	www.achaogen.com
AzurRx BioPharma	Brooklyn, NY	Nasdaq: AZRX	36	www.azurrx.com
Anatara			13	

Antimicrobial Drug Developers

Achaogen. This company develops new antibacterials for the treatment of gram-negative infections. The firm's leading compound, Zemdri (plazomicin), is approved in the US for complicated urinary tract infections, as well as Enterobacteriaceae infections. Its second product, C-Scape, is a beta-lactam/beta-lactamase inhibitor that is being evaluated in complicated urinary tract infections due to MDR pathogens.

CorMedix. It is working on a new formulation of taurolidine, an antimicrobial agent that was originally used in the local treatment of peritonitis but was subsequently shown to be effective in the prevention of catheter-related bloodstream infections. CorMedix's product Neutrolin is non-antibiotic and anti-infective, and combines taurolidine with heparin to decrease the threat of infections and blood clots. Neutrolin, CE-marked in Europe, is in Phase III development for patients undergoing chronic hemodialysis via a central venous catheter in the US.

Paratek Pharmaceuticals. This firm, co-founded by Nobel laureate Wally Gilbert, is developing Nuzyra (omadacycline) – the first in a new class of antibiotics called the aminomethylcyclines approved in the US. The drug is approved for two indications – community-acquired bacterial pneumonia, and acute bacterial skin and skin structure infections. Paratek's second product – a once-daily oral tetracycline-derivative Sarecycline – has also received NDA approval in inflammatory acne.

Tetraphase Pharmaceuticals. It is evaluating a synthetic chemistry platform inspired by the core chemical structure of tetracycline. The company's leading

Eravacycline compound, a fully synthetic tetracycline antibiotic, has been approved by the US FDA for the treatment of complicated intra-abdominal and urinary tract infections.

Animal Health Companies

Aratana Therapeutics. This company develops medicines for pets suffering from chronic diseases. It has three US FDA-approved products – Entyce, a selective ghrelin receptor agonist for appetite stimulation in dogs; Nocita, a bupivacaine local anesthetic formulation for dogs; and Galliprant, a prostaglandin receptor antagonist for canine pain and inflammation associated with osteoarthritis.

ECO Animal Health Group. This UK-based global animal health company has a patented drug Aivlosin – a macrolide antibiotic for treating respiratory and enteric diseases in pigs and poultry. The firm also develops multiple generic drugs for the treatment and prevention of parasites in cattle, sheep, pigs, horses, and dogs.

Kindred Biosciences. This firm repurposes human products for use in veterinary medicine. It is developing monoclonal antibodies and recombinant proteins for diseases such as GI disorders, including equine gastric ulcers and IBD in dogs. The company has already launched Mirataz – a transdermal ointment – to deliver the antidepressant mirtazapine as an appetite stimulant for cats and is preparing to launch Zimeta, an injectable version of the pain drug Metamizole for treating fever in horses.

Oasmia Pharmaceutical. This Swedish firm manufactures products for human and animal oncology. Its leading program is Apealea (a formulation of paclitaxel) and Doxophos (a formulation of doxorubicin) is another program. These products are already approved in Russia (Apealea for ovarian cancer and Doxophos for all cancer indications) for human use. Apealea has also received positive CHMP opinion in the EU and the Orphan Drug Designation in the US. A veterinary version of these products is currently being developed under the names Paccal Vet-CA1 and Doxophos Vet, respectively.

Human GI Disorder Drug Development Companies

Ardelyx. This company has a pipeline of gut-restricted therapies for the treatment of cardiorenal and GI diseases. The most advanced GI program is evaluating the potential of Tenapanor, an NHE3 inhibitor, in Phase III studies for IBS-C. The firm is also evaluating an early-stage NHE3 inhibitor for potential use in GI indications.

AzurRx BioPharma. This clinical-stage biopharma company is developing recombinant proteins for the treatment of GI diseases and microbiome-related conditions. It has two early-stage pipeline products – MS1819 and AZX1101. The former is a recombinant lipase being studied for the treatment of exocrine pancreatic insufficiency (cystic fibrosis and chronic pancreatitis), while the latter is a recombinant enzyme for the prevention of hospital-acquired C.*difficile* infections.

Protagonist Therapeutics. This clinical-stage biopharma firm is developing peptide-based new chemical entities. Its pipeline includes early-phase GI-restricted peptides (PTG-100 and PTG-200) for IBD and injectable peptides (PTG-300) for rare blood disorders. PTG-100 is a α4β7 integrin-specific antagonist being evaluated for the treatment of ulcerative colitis in a Phase II trial, while PTG-200 is an IL-23R antagonist for the potential treatment of Crohn's disease in a Phase I trial.

Nutraceuticals

AB-Biotics. This Spain-based biotech company offers probiotics in segments such as cardio-metabolism, oral care, pediatrics, gastrointestinal, gynecology, urology, dermatology, and immunology.

Biosearch. This Spain-based firm is developing three products in the pharma, nutraceutical, and functional food sectors. These products include Hereditum, premium probiotics isolated from human breast milk for infant nutrition; Eupoly-3, a line of EPA- (eicosapentaenoic acid) and DHA- (docosahexaenoic acid) rich ingredients designed for use as food supplements; and Exxentia, a line of plant extracts.

ChromaDex. This nutraceutical company markets its flagship ingredient Niagen (nicotinamide riboside) for healthy aging. This product is used by cells to create nicotinamide adenine dinucleotide (NAD+) – an essential molecule found in every living cell. The firm is also promoting Immulina (a spirulina extract for boosting the immune system) and Anthorigin (water-extracted, non-GMO purple corn husk extract with a healthful antioxidant compound called anthocyanin).

Appendix VII – Risks for Anatara

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

- **Clinical risk.** There is the risk that GaRP fails to demonstrate expected benefits in efficacy studies for IBD and IBS given the complexity of these diseases.
- **Partnering risk**. There is the risk that Anatara fails to secure a partner for GaRP within the stipulated timelines.
- **Funding risk**. There is the risk that Anatara's current cashflow exhausts faster than expected and that it does not get enough funding to survive itself through R&D efforts in human GI health.
- **Timing risk**. Zoetis' commercialization efforts for Detach may be delayed impacting the royalty on product sales that Anatara expects. Also, efficacy studies with GaRP may take longer than expected.

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 cognizant of the abovementioned specific and general risks before buying any the stock of any biotechnology and medical device stock mentioned on this report, including Anatara.

General advice warning, Disclaimer & Disclosures

Terms & Conditions

The information contained herein ("Content") has been prepared and issued by Pitt Street Research Pty Ltd ACN 626365615 ("Pitt Street Research"), an Authorised Representative (no: 1265112) of BR Securities Australia Pty Ltd. ABN 92 168 734 530, AFSL 456663. All intellectual property relating to the Content vests with Pitt Street Research unless otherwise noted.

Disclaimer

The Content is provided on an as is basis, without warranty (express or implied). Whilst the Content has been prepared with all reasonable care from sources we believe to be reliable, no responsibility or liability shall be accepted by Pitt Street Research for any errors or omissions or misstatements howsoever caused. Any opinions, forecasts or recommendations reflect our judgement and assumptions at the date of publication and may change without notice. Pitt Street Research will not accept any responsibility for updating any advice, views, opinions or recommendations contained in this document.

No guarantees or warranties regarding accuracy, completeness or fitness for purpose are provided by Pitt Street Research, and under no circumstances will any of Pitt Street Research officers, representatives, associates or agents be liable for any loss or damage, whether direct, incidental or consequential, caused by reliance on or use of the Content.

General Advice Warning

The Content has been prepared for general information purposes only and is not (and cannot be construed or relied upon as) personal advice nor as an offer to buy/sell/subscribe to any of the financial products mentioned herein. No investment objectives, financial circumstances or needs of any individual have been taken into consideration in the preparation of the Content.

Financial products are complex, entail risk of loss, may rise and fall, and are impacted by a range of market and economic factors, and you should always obtain professional advice to ensure trading or investing in such products is suitable for your circumstances, and ensure you obtain, read and understand any applicable offer document.

Disclosures

Pitt Street Research has been commissioned to prepare the Content. From time to time, Pitt Street Research representatives or associates may hold interests, transact or hold directorships in, or perform paid services for, companies mentioned herein. Pitt Street Research and its associates, officers, directors and employees, may, from time to time hold securities in the companies referred to herein and may trade in those securities as principal, and in a manner which may be contrary to recommendations mentioned in this document.

Pitt Street Research receives fees from the company referred to in this document, for research services and other financial services or advice we may provide to that company. The analyst has received assistance from the company in preparing this document. The company has provided the analyst with communication with senior management and information on the company and industry. As part of due diligence, the analyst has independently and critically reviewed the assistance and information provided by the company to form the opinions expressed in the report. Diligent care has been taken by the analyst to maintain an honest and fair objectivity in writing this report and making the recommendation. Where Pitt Street Research has been commissioned to prepare Content and receives fees for its preparation, please note that NO part of the fee, compensation or employee remuneration paid will either directly or indirectly impact the Content provided.