ASX Release

Anatara Lifesciences - Operational update

- **Revised protocol for Irritable Bowel Syndrome (IBS) trial of "GaRP" successfully implemented with ongoing review of recruitment and enrollment processes**
- **Additional trial measures to enhance participant support and access, including further sites with Royal Melbourne Hospital now recruiting**
- **Result of recent trial of ANR-pf(poultry) with major Australian producer inconclusive and discussions remain ongoing**

MELBOURNE, 11 August 2022: Anatara Lifesciences (ASX: ANR or "the Company"), a developer of evidence-based solutions for gastrointestinal diseases in humans and animals, is pleased to provide an important operational update. The Company continues to review the progress of human trials, inclusive of all processes.

GaRP – Irritable Bowel Syndrome (IBS) - Trial Update

The previous ASX announcement referred to re-contacting "more than 300 potential participants with the others and new applicants to be processed in coming weeks" for the new broader "GaRP" (Gastrointestinal Re-Programming complementary medicine) trial criteria of IBS modified to exclude only the constipation subset. This led to an improvement in conversion from interest to enrolment, and the Company has been closely monitoring the ongoing momentum of both patient interest and conversion into trial participation. While the participant numbers are short of the recruitment milestone anticipated by this point after the broadening of IBS patient criteria, there are now approximately 20% of the required 90 patients for the interim readout enrolled and growing.

Anatara's executive chair, Dr. David Brookes commented: "Anatara, like many other biotechnology companies, has been challenged with trial recruitment over the last year or so. While being disappointed to be behind in our anticipated recruitment milestone following the broadening of the GaRP trial criteria, our team is confident that the findings of the continuing review process will allow ongoing momentum with enrolment. We are encouraged by the mainstream support for the quality and relevance of the GaRP trial and of other projects being assessed."

Anatara continues to review and consider additions and potential adjustments to the current GaRP trial procedures, including a review to simplify the participant data collection processes. The current recruitment rate and reinforcement will likely result in interim results from the first arm being delayed with a new release date set for CY1Q2023.

The Royal Melbourne Hospital is the latest site which has been approved and onboarded as a recruitment site for the IBS trial. The recent initiation will assist the GaRP trial progress with potential participants already in screening. Additional sites and services to make participation in the trial easier, are being considered internally with a view to enhance recruitment and compliance.

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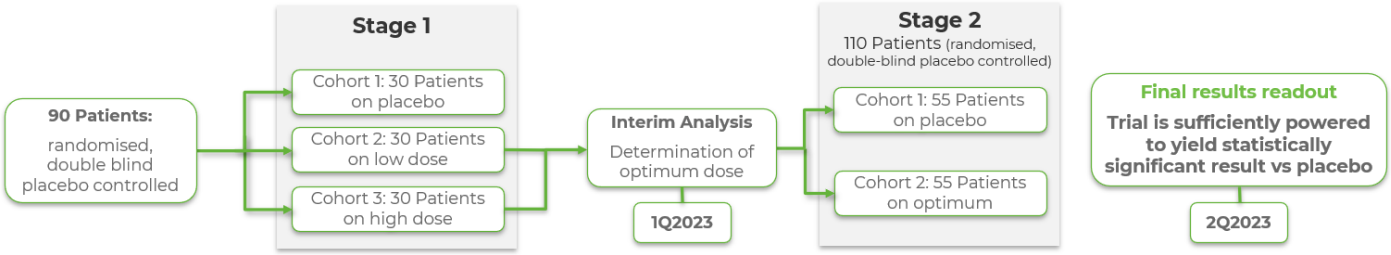
The GaRP IBS trial is designed to deliver powered results that will validate support claims. If successful, the high prevalence of digestive disorders requiring relief from both symptoms and the disease process, including irritable bowel syndrome (IBS), present a significant market opportunity for Anatara.

The commercial opportunity for non-prescription products for gastrointestinal disorders and IBS is US$8 billion in the US[2]

GaRP – Irritable Bowel Syndrome (IBS) – Clinical Trial Design



Animal Health Update

Anatara had previously advised in ASX release 22nd June 2022 of an extensive in-field poultry treatment trial and potential collaborative directions for the commercial delivery of the porcine product. The Company can now update the poultry trial result with a leading Australian producer using ANR-pf (poultry) in broilers (chickens for meat production). This most recent trial delivered mixed results that suggested to both parties that a commercial product pathway requires further investigation. These considerations have been agreed for ongoing discussion in the near future. The need to address antimicrobial resistance across animal production remains a strong focus in the industry.

3FDC - Psychological functioning trial

As previously advised, the psychological functioning study is being conducted by the CSIRO using 3FDC. The trial is in the process of recruiting ~100 patients with with mild to moderate levels of depression, anxiety, or stress symptoms indicated by the Depression, Anxiety and Stress Scale (DASS-21).

There is increasing interest in the "gut-brain" axis and the influences of the microbiome. The GaRP complementary medicine includes a subset of 3 components formulated for release in the lower large intestinal tract which have been labelled "3FDC".

The trial aims to explore the effectiveness of 3FDC for improved mental health. If successful, the market opportunity is significant with the global brain health supplements market expected to reach US$15.74 billion by 2030, registering a CAGR of 8.3% from 2022 to 2030. The market growth is largely attributed to the increasing awareness about mental health issues, including, attention, focus, depression, and anxiety.[1]

Anatara anticipates being able to update the progress of this trial with the CSIRO this quarter.

For more information please contact:

[1] https://www.grandviewresearch.com/press-release/global-brain-health-supplements-market

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About Anatara Lifesciences Ltd

Anatara Lifesciences Ltd (ASX: ANR) is developing and commercialising innovative, evidence-based products for gastrointestinal health where there is significant unmet need. Anatara is a life sciences company with expertise in developing products for human and animal health. Anatara is focused on building a pipeline of human gastrointestinal health products. Underlying this product development program is our commitment to delivering real outcomes for patients and strong value for our shareholders.

Background information & Appendices

Human Trials

Dose Determination and Efficacy Evaluation of the Gastrointestinal ReProgramming (GaRP) Dietary supplement in Irritable Bowel Syndrome

"GaRP" is the working name for Anatara's evidence-based complementary medicine that includes unique formulations of bromelain, an enzyme extracted from pineapple stems, along with other synergistic GRAS[4] components. The combination and coating of these GaRP components have a beneficial effect on the physiology of the gastrointestinal lining, a positive influence on the microbiome (homeostasis & metabolites) and allow absorption of beneficial components in targeted areas of the gastrointestinal tract.

This randomised, double-blinded, placebo-controlled study, commenced in August 2021, is being conducted in two stages as a virtual study. This involves minimal on-site visits and participants completing assessments online. Up to 6 sites will be established and 200 participants enrolled. The study design consists of two stages with an interim analysis between stages. Stage 1 is now anticipated to be completed in early 1st quarter of calendar 2023 followed by interim results soon thereafter. Stage 2 is anticipated to be completed in 2nd quarter of calendar 2023.

Stage 1 will assess safety, tolerability, and be a guide to the efficacy of the two different strengths of GaRP used against a placebo, randomly divided in a protocol of 3 equal groups. Following interim analysis, one dose will be selected, and the remaining participants recruited in a 1:1 randomisation protocol. Of the 200 planned participants, at least 90 will enrol in stage 1, and 110 participants will enrol in stage 2. For each participant in each stage, the study will last for 12 weeks; including 8 weeks of treatment, preceded by a 2-week screening/baseline period, and followed by a 2-week washout period. Measurements will include a number of surveys including the IBS specific surveys: IBS-SSS (severity scoring system), IBS-AR (adequate relief) and Bristol Stool Form Scale. Other surveys will look at overall well-being, such as the IBS QoL (quality of life) and HADS (Hospital Anxiety and Depression Scale) in recognition of the importance of the gut-brain connection. The usual and expected clinical markers will all be monitored, including microbiome analysis.

Irritable Bowel Syndrome (IBS) is the most diagnosed gastrointestinal condition and a significant burden on healthcare. Over US$8 billion is spent annually on supplements and OTC digestive remedies in the US alone, presenting a huge market opportunity for Anatara. Our human health products will be built on strong scientific foundations for credibility and consumer confidence that provides a marketing distinction. The pre-clinical data to support the use of GaRP is very robust and our expectation is that this will translate in the human IBS trial. The trial includes all sub-types of IBS except subtype C, which is sub-type with constipation as the predominate symptom.

The website for registering interest in this trial can be found at: https://trials.evrima.com.au/irritable-bowel-syndrome-ibs-medical-study-registration

CSIRO trial –the "Gut-brain connection "using Anatara's 3FDC from GaRP pipeline

Anatara's GaRP pipeline not only addresses GIT homeostasis but more general harmony and well-being through influences on the gut -brain connection. "3FDC" is the Company's working reference to specific components from the overall GaRP product that are coated for targeted release beyond the small intestine to allow delivery and influence in the large intestine. The 3FDC components are anticipated to have direct and indirect effects including assisting the homeostasis of a healthy microbiome. The delivery of these components and the microbiome influences are considered important for gut-brain axis balance, hence the 3FDC components have been selected to explore their effect on depression, anxiety, and stress symptoms in otherwise healthy individuals.

In partnership with the CSIRO, Anatara is utilising 3FDC as a specific complementary medication to explore these effects (on depression, anxiety, and stress-related symptoms in otherwise healthy individuals) with the implied method of action being absorption of key components, a positive influence on the microbiome homeostasis and assisting the gut wall function.

The study into the effects of 3FDC in adults with moderate anxiety, stress or depression commenced in February 2022 and is anticipated to be completed by 1st quarter of calendar 2023. This randomised, double-blinded, placebo-controlled study is being conducted at CSIRO's Nutrition and Health Research Clinic in Adelaide. The study will recruit 100 participants to be randomised into two arms in a 1:1 ratio to treatment with 3FDC or placebo which is dosed twice a day for 6 weeks. Participants will be assessed at the start and end of the study period 'in-clinic' and will complete a series of questionnaires on a customised smartphone app over the duration of the study. In the event of tightening COVID-19 restrictions impacting 'in-clinic' visits, the study will transition to a virtual study with telehealth consultations. Such a transition is not anticipated to impact the primary outcome. The primary outcome is a clinically significant reduction in Hospital Anxiety and Depression Scale (HADS) scores. The study is powered at ~95% to detect a clinically relevant reduction of ≥1.5 points in HADS scores from baseline to end of treatment (6 weeks) Secondary outcomes include mood and wellbeing questionnaires, gut symptom ratings and blood plasma markers**.**

The website for registering interest in this trial can be found at: https://www.csiro.au/en/work-with-us/industries/health/Nutrition-and-health-research-clinic/Dietary-supplement-psychological-health

1. The DASS is a quantitative measure of distress along the three axes of depression, anxiety[a] and stress[b]. It is not a categorical measure of clinical diagnoses; a. Symptoms of psychological arousal; b. The more cognitive, subjective symptoms of anxiety.
2. Mintel's 2018 Digestive Health U.S. – July
3. NBJ Nutrition Business Journal Feb 22, M.Juntti, A.Wong, Stressed and Sleepless. Page 11-14
4. Generally Recognised As Safe – US FDA designation that a substance is considered safe for use in food

Animal Trials

The efficacy of ANR-pf on the performance of broilers subject to a subclinical necrotic enteritis challenge was previously announced to the ASX on 1st February 2021 and has been the basis for ongoing confidential trials in commercial poultry production.

The trial detailed the inclusion of a total of 540 Ross male chicks with lighting, relative humidity, temperature and treatment diets that followed Ross 308 guidelines. The birds were randomly allocated to treatments and pens. Challenge groups were inoculated with a necrotic enteritis challenge. Non-challenge groups were inoculated with sterile control.

A positive effect during the grower period (days 10-24) was observed with the treatment of ANR-pf added in the drinking water, where the birds receiving the product in drinking water showed a significantly higher weight gain compared to all other challenged birds. The overall performance of birds (days 0-35) showed improved weight gain of the challenged birds receiving the product in water and did not significantly differ with the non-challenged birds. Oocyst shedding was also lower in this group compared to the untreated challenged birds.

When analysed over the entire experimental period (days 0-35), treatment with ANR-pf in water provided benefit when compared to untreated birds in weight gain($p=0.007$), feed intake ($p=0.039$), as well as lesion scores in both the jejunum ($p=0.040$) and ileum ($p=0.035$), and oocyst shedding ($p<0.05$). The difference in feed conversion rate also improved, although failed to reach statistical significance.

The study showed that the ANR-pf applied in drinking water had potential to be considered a useful additive, especially on necrotic enteritis occurrence. This suggested further studies to determine if dose and dosing regimen could improve such positive effects on bird health and performance.

Following this successful challenge study announced in early 2021, Anatara has been collaborating with a leading producer to conduct confidential trials.

Authorised by: The Board of Anatara Lifesciences Ltd.

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