ASX Release

Anatara Lifesciences provides Clinical Trial and Operational update

- **Revised protocols for Irritable Bowel Syndrome (IBS) and psychological functioning trials successfully implemented with associated increases in enrollment**
- **Operational update**

MELBOURNE, 22 June 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 update on the progress of clinical trials in irritable bowel syndrome and psychological functioning. The Company also provides a brief operational update.

Human clinical trials for IBS (GaRP) and psychological functioning (3FDC)

Globally there is a high prevalence of digestive disorders requiring relief from both symptoms and the disease process, including irritable bowel syndrome (IBS). There is also increasing interest in the "gut-brain" axis and the influences of the microbiome. The "GaRP" and "3FDC" complementary medicines provide a significant market opportunity to address these considerations whilst improving individuals' quality of life.

CEO Steve Lydeamore commented: "On 20 May 2022, the Company advised that it was updating the recruitment website and Obvio Health ClaimIt online portal and mobile app for the IBS trial in advance of re-screening more than 300 potential participants who were unable to enrol due to not having diarrhoea predominant IBS. Anatara has completed the updates of the website, portal and mobile app.

As of the end of last week, we have re-contacted 306 of those potential participants, with these and new applicants to be processed in coming weeks. We anticipate interim results in 4Q2022 and final results in 1Q2023.

We continue to work through the approval process for adding the previously advised Melbourne site for the IBS trial. We anticipate site initiation in 3Q2022 which will be timely for that stage of the GaRP trial progress. Currently the team is at maximal capacity processing applicants for the immediate weeks ahead.

The revised protocol for the psychological functioning (3FDC) study has been implemented and the recruitment rate has increased as a result. We anticipate final results in 1Q2023. To date, the dosage form has been well tolerated and there have been no investigational product related serious adverse events."

The commercial opportunity for non-prescription products for gastrointestinal disorders and IBS is US$8 billion in the US[1], whilst the non-prescription mood and mental health category is a substantial opportunity with annual growth of 30% in the US[2].

1. Mintel's 2018 Digestive Health U.S. – July
2. NBJ Nutrition Business Journal Feb 22, M.Juntti, A.Wong, Stressed and Sleepless. Page 11-14

Anatara Lifesciences Limited
Registered Office
Level 3, 62 Lygon Street, Carlton South, VIC, 3053, Australia
Administration and R&D
Suite 101, 55 Flemington Rd, North Melbourne, VIC 3051, Australia
Email info@anatara.com | Website anataralifesciences.com

Operational update

Anatara's chair, Dr. David Brookes added: "The transition and handover in advance of the CEO's departure in late June has included visiting the facilities at the CSIRO Nutrition and Health Research Clinic in Adelaide. This site is undertaking the psychological functioning (3FDC) trial and also participating as a site in the IBS (GaRP) trial.

The leaders of the 3FDC trial are clinical psychologists with a long-term interest and deep understanding of the role of the gut-brain axis as an influence on psychological well-being. As expected, the facilities were very impressive and incredibly accommodating for trial participants. (*Please see details on the trial website links below)*

Mr. John Michailidis has now joined the Anatara team as Chief Operations Officer (COO). As part of the handover, we have recently met with key opinion leaders in the gastrointestinal field. There remains a pleasing level of interest in both the current trials and potential future trials in paediatric participants and other gastrointestinal diseases and disorders.

We anticipate being able provide an update on the animal health products, ANR-pf (poultry) and BONIFF (pigs) in the earlier part of 3Q2022, with results of an extensive in field poultry trial and potential collaborative directions for a commercial delivery of the pig product. While the focus is on human health projects including ongoing assessment of other evidence-based solutions to address unmet needs, we remain committed to endeavouring to realise value from the animal health assets."

Background information

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[3] 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 approximately 200 participants enrolled. The study design consists of two stages with an interim analysis between stages. Stage 1 is anticipated to be completed early in the 4th quarter of calendar 2022. Stage 2 is anticipated to be completed in 1st 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

3. Generally Recognised As Safe – US FDA designation that a substance is considered safe for use in food

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. Approximately 100 participants will be randomised in a 1:1 manner 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) with significance set at 5% ($\alpha = 0.05$; $\beta = 0.95$; $f=0.15$). 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**

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.

Anatara Lifesciences Limited
Registered Office
Level 3, 62 Lygon Street, Carlton South, VIC, 3053, Australia
Administration and R&D
Suite 101, 55 Flemington Rd, North Melbourne, VIC 3051, Australia
Email info@anatara.com | Website anataralifesciences.com

For more information please contact:

Dr. David Brookes
Chair, Anatara Lifesciences Ltd
+61 (0) 411 712 579
dbrookes@anatara.com

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.