ASX Release

Anatara announces Positive Results from Stage 1 of the Irritable Bowel Syndrome (IBS) clinical trial

Highlights

- The interim analysis of the Stage 1 sixty-one (61) Intent-to Treat (ITT) patient group has been finalised in the GaRP Irritable Bowel Syndrome (IBS) trial with the recommendation that the trial should continue to Stage 2 using the Low Dose.
- The interim analysis and Data Safety Monitoring Board (DSMB) review confirmed that Stage 1 successfully met the study objectives of confirming safety and the optimum dose for the single dose expanded Stage 2 of the Phase I/II trial with a preliminary indication of meaningful efficacy.
- Stage 1 analysis of the cohort of participants on low dose showed an improvement from the baseline in the internationally recognised Irritable Bowel Severity Scoring System (IBS-SSS) of 56% reduction after 8 weeks treatment (the high dose returned a 50% reduction). The low dose cohort outperformed the placebo group by approximately 20% over the 8 weeks of randomization.
- The primary endpoint of the GaRP-IBS Trial is a clinically meaningful reduction in the internationally recognised IBS-SSS and secondary endpoints include improvements in quality of life, anxiety and depression. Stage 1 secondary endpoints are still currently being analysed.
- Stage 1 of the GaRP-IBS Phase I/II Trial consisted of 3 cohorts (Placebo, Low Dose & High Dose) in a randomised, double blind, placebo-controlled study.
- The Company believes today's results are encouraging enough to explore the process to registration of GaRP in Australia and other jurisdictions as a clinically validated IBS treatment.
- The Company anticipates strong commercial interest in these interim results given the clear unmet need for non-prescription products to relieve and modify gastrointestinal disorders such as IBS. The global Digestives and Intestinal treatments market amounts to US$18.64bn in 2023.[1]

Adelaide, 28 September 2023: Anatara Lifesciences (ASX: ANR or "the Company"), a developer of evidence-based solutions for gastrointestinal diseases in humans and animals, is pleased to announce it has met the study objectives of Stage 1 of its Gastrointestinal ReProgramming (GaRP) trial for IBS and the

[1] https://www.statista.com/outlook/cmo/otc-pharmaceuticals/digestives-intestinal-remedies/worldwide

Data Safety Monitoring Board (DSMB) has recommended that the Company should proceed with Stage 2 using the Low Dose as the optimum dose.

GaRP – Irritable Bowel Syndrome (IBS) Phase I/II trial

Anatara's GaRP product is a multi-component, coated complementary medicine designed to address underlying factors associated with chronic gastrointestinal conditions such as IBS and IBD. The product consists of GRAS (Generally Regarded As Safe) components and is designed to assist restoration and maintenance of the gastrointestinal tract (GIT) lining and the homeostasis of the microbiome.

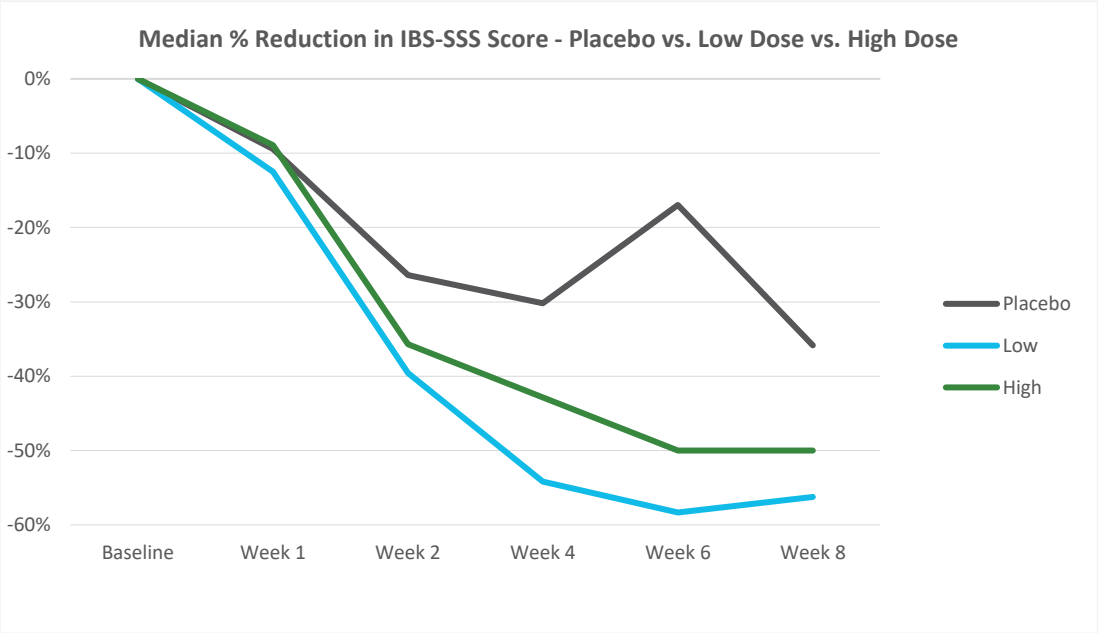
The interim futility statistical analysis of Stage 1 of the GaRP-IBS trial was reviewed by the DSMB (Data Safety Monitoring Board) on 27 September 2023 and concluded that Stage 1 has successfully met the study objectives of confirming safety and the optimum dose for the single dose expanded Stage 2 of the trial, with a preliminary indication of meaningful efficacy. The data from 61 participants over 3 arms (placebo, low and high dose) strongly supported continuing the trial using the Low Dose. There were no concerning safety signals and the DSMB were satisfied that continuation of the current trial protocol was supported. The DSMB have suggested considering variations to the randomisation in Stage 2 to aid recruitment by considering reduction of the placebo rate, e.g. increasing randomisation ratio to 2:1 optimum dose vs placebo, as opposed to the currently proposed 1:1 (optimum dose vs placebo) randomisation.

Anatara's Executive Chair, Dr David Brookes commented that "*This is a very pleasing and not unexpected outcome from the Stage 1 interim analysis given the trial design. To confirm safety and the optimum dose with a meaningful indication of efficacy was the intention of Stage 1 of the trial. The Company is buoyed by this milestone and looks forward to advancing the GaRP project. Encouragingly the reduction in symptoms using the IBS-SSS suggests a meaningful adjunctive treatment for those patients meeting the criteria for moderate IBS. More broadly our expectation is that this complementary medicine's rejuvenating gastrointestinal tract (GIT) effects will provide relief for sufferers of non-specific GIT symptoms and be an adjunctive therapy in other medical indications, such as IBD (Inflammatory Bowel Disease). As previously highlighted, the trial was more challenging than anticipated and highlighted the difficulties that sufferers of IBS deal with from day to day. The Company has learnt from these tribulations and I feel is now well placed to efficiently conduct Stage 2. We are also looking forward to sharing the data and discussing the results with other corporates and already interested potential partners following the analysis of Stage 1 of the IBS trial.*"

Headline Data Overview – Stage 1

The below chart highlights that GaRP is having a clinically meaningful reduction in trial participants' IBS-SSS Scores. It is highly encouraging to see such a strong divergence between Placebo and the active Low and High Dose arms, as this provides solid evidence that the drug is having an effect (working) whereas placebo is not.
As is the case with statistical analysis, increasing the population/patients in the trial (as is proposed for stage 2 of the study) is expected to provide statistically significant P values.

The statistical analysis suggests that Stage 2 may require as few as a total of 50 participants on the optimum Low Dose of product versus the placebo group to achieve the desired primary endpoint of at least a 20% improvement (reduction) in IBS-SSS Scores, noting that this 20% reduction has been achieved in Stage 1.



The below table details the median IBS-SSS Scores for Stage 1 and highlights the large positive change in patients' IBS scores on the two drug arms (high and low dose). To achieve a 50%+ reduction in one's IBS Score translates to a significant positive change in day-to-day life, a benefit that cannot be understated. An IBS-SSS score of 240 is toward the high end of moderate IBS whilst 140 is mild IBS.

Median IBS-SSS Score – Baseline to week 8			
	Placebo	Low	High
	n=20	n=20	n=21
Baseline	265	240	280
Week 1	240	210	255
Week 2	195	145	180
Week 4	185	110	160
Week 6	220	100	140
Week 8	170	105	140
Difference baseline score to week 6 score	45	140	140
%	-17%	-58%	-50%
Difference baseline score to week 8 score	95	135	140
%	-36%	-56%	-50%

The IBS Symptom Severity Scale (IBS-SSS) is a global measure of IBS symptoms that aggregates patient ratings of different, well-defined domains of IBS into a single overall score. The measure is utilised in clinical trials to monitor the progress of the disease and treatment effect. A score below 75 is seen in healthy people or those in remission, whilst 75–175 indicates mild disease, 175–300 moderate disease and over 300 indicates severe disease. The Anatara GaRP-IBS trial recruited patients with scores in the 175-350 range.

The Company notes the difficulties for patients on placebo in the trial for the full duration with patients suffering from difficult to manage symptoms tending to drop out. The dropping out of 3 placebo patients from week 6 to week 8 highlights this, whilst the low or high dose arm from week 6 to week 8 participation remained stable.

This point is reinforced by the week 6 Placebo response showing a strong return to baseline, something that would be expected for placebo, giving the Company optimism that larger patient numbers in Stage 2 would be likely to show a placebo trend of returning to baseline in week 8 as it did for week 6.

The Company is not surprised or concerned about the high placebo response as the medical literature shows that IBS clinical trials typically have a high placebo response on average of about 40%, very much in line with today's results[2].

The outperformance of the low-dose over the high-dose enhances the potential clinical utility of GaRP in a commercial setting. In terms of safety and ultimate commercial attractiveness of the product, achieving the desired clinical utility with a lower dose is preferred for the following reasons:

- Lower dose means less drug which means less chance of safety concerns or unwanted side effects,
- Less drug needs to be manufactured per patient dose and this has obvious cost savings and improved margins, and
- Less chance of other drug to drug interactions.

Anatara's objective is to advance the clinical development plan for GaRP as an effective treatment for IBS and bring the product to market, part of which means registering the product with Therapeutic Goods Association of Australia (TGA) and other jurisdictions. The Company will consider regulatory advice and processes towards achieving approval given today's positive human safety and efficacy data and the GRAS nature of GaRP's ingredients.

The Company has engaged with numerous corporates and companies ranging from the Speciality Pharmaceutical to Vitamin & Wellness sectors regarding potential partnering. These companies are interested in expanding their portfolio of complementary medicines and recognise the substantial global opportunity in gut health, the microbiome and the importance of the role that the gut-brain axis plays in human health and well-being.

[2]https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6414074/#:~:text=Estimates%20of%20the%20placebo%20response,approximately%2040%259%E2%80%9311.

Large Unmet Need for an effective IBS Treatment

GaRP presents itself as a potential disease-modifying treatment that aims to positively impact a substantial proportion of the population that suffer from the debilitating symptoms of digestive disorders, including irritable bowel syndrome (IBS).

The lack of efficacious digestive treatments amplifies the clear unmet need and the significant market opportunity for Anatara. The global Digestives & Intestinal treatment market amounts to US$18.64bn in 2023.[3] Furthermore, GaRP is restorative of the gastrointestinal tract lining and benefits the homeostasis of the microbiome which are beneficial effects for the complex gut-brain axis.[4]

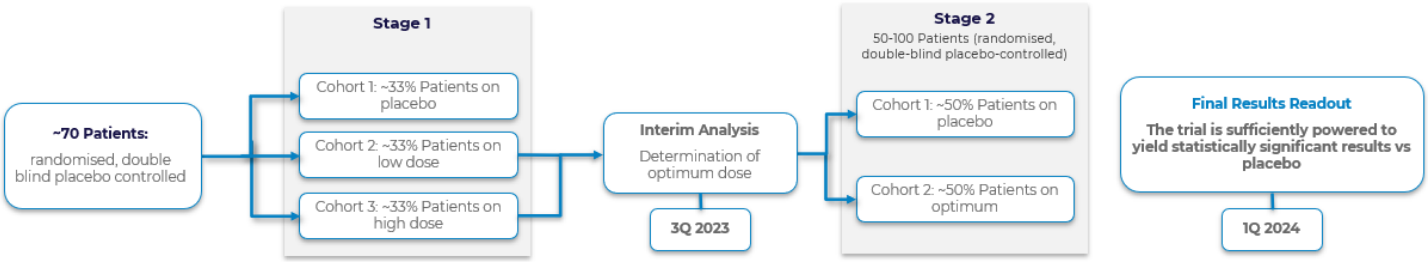
Trial Design – Stage 1

Recruitment for Stage 1 was finalised in June with approximately 70 patients from the more than 2,700 applicants screened for enrolment. The GaRP-IBS trial is powered to deliver results that will validate and support efficacy claims. There were 61 Intent to Treat patients in the final Stage 1 interim analysis with some other participants not included after withdrawing/not complying following the randomisation stage.

The trial enrolled males and females 18-65 years of age with irritable bowel syndrome (IBS-SSS score of 175-350). Patients were dosed twice daily for 12 weeks.

The trial has been designed to return, if successful, a clinically meaningful and statistically significant result, with primary endpoints of a reduction in the IBS-SSS (Irritable Bowel Severity Scoring System) and safety. Secondary endpoints include quality of life, anxiety and depression and pain improvements.

GaRP-IBS Clinical Trial Design



[3] https://www.statista.com/outlook/cmo/otc-pharmaceuticals/digestives-intestinal-remedies/worldwide

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

Key endpoints for the Trial

Primary Endpoints	Secondary endpoints
• Change in IBS-Severity Scoring System (IBS-SSS) between test and placebo groups compared to baseline • Treatment-Related Adverse Events	• IBS Adequate Relief (IBS-AR) compared to baseline • Hospital Anxiety and Depression (HAD) Scale comparing to baseline • Change in IBS quality of life (IBS QoL) points compared to baseline • Safety markers
Exploratory Endpoints	
• Plasma levels of specific inflammatory markers • Use of rescue medication across the study group	• Alterations in gut microbiota with respect diversity and balance; correlation to IBS symptoms including overall wellness

Ongoing corporate initiatives

The Company continues to actively assess other opportunities in the human healthcare space and is appraising projects suitable to add to the Company's portfolio. Today's positive results reinforce that the GaRP product can be a meaningful treatment for not only IBS patients but for symptomatic relief of GIT health sufferers who do not meet a diagnostic criteria. As well, the Company has established interest for other mainstream indications to use GaRP as adjunctive therapy, such as IBD (Inflammatory Bowel Disease) The Company will continue to focus efforts on partnering and progressing the trial to Stage 2. There are also ongoing discussions for potential uses of Anatara's established products and know-how for animal health indications.

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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.

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