

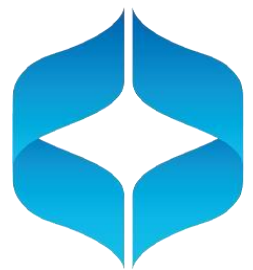
ASX Release

## Phase II GaRP-IBS (Irritable Bowel Syndrome) trial Headline analysis of results following completion of Stage 2

### Highlights

- Following the completion of Stage 2 of Anatara's GaRP-IBS (Irritable Bowel Syndrome) Phase II trial, the headline results analysis confirms no safety concerns and that the primary endpoint for efficacy of a reduction in IBS-SSS versus placebo was not met, despite a consistent and meaningful response being observed during the trial.
- The secondary endpoint of improvement in anxiety scores reached statistical significance (P-value 0.034, Week 8), which influenced the significance of the overall HADS score (P-value 0.025 at Week 8), with depression scores remaining stable (within normal range). "HADS" being the commonly used Hospital Anxiety Depression Scale.
- The IBS-SSS ("SSS" Symptom Scoring System) experienced a consistent and sustained improvement, with a reduction of more than 40% observed in the trial, but this did not reach statistical significance when compared to placebo. Another secondary endpoint of a 20% or more reduction (improvement) in IBS-SSS compared to baseline in the cohort on the GaRP product was clearly achieved.
- Pleasingly, the secondary endpoint of IBS-Adequate Relief was highly significant at 10 weeks with a P-value 0.004, indicating the self-assessment of participants as "responders" clearly outweighed "non-responders" versus placebo.
- The Company is considering future directions and opportunities, with further cashflow controls, following the trial outcome of a negative primary efficacy endpoint. The GaRP project value within the robust pre-clinical IBD (Inflammatory Bowel Disease) studies and the positive outcomes from the GaRP-IBS trial will be formalised for commercial considerations.
- The GLP-1 agonism focused "Anti-Obesity Project" proof-of-concept pre-clinical mice studies have commenced at the university involved, with the project scope to be further determined by observations and milestones within 6 months.

ADELAIDE, 17 April 2025: Anatara Lifesciences (ASX: ANR or "the Company"), a developer of evidence-based, innovative products to address significant unmet need in human health, with a particular focus on conditions that involve the complexity of the gastrointestinal tract (GIT), provides details on the Company's GaRP-IBS trial analysis, an update on the anti-obesity project and current activities.



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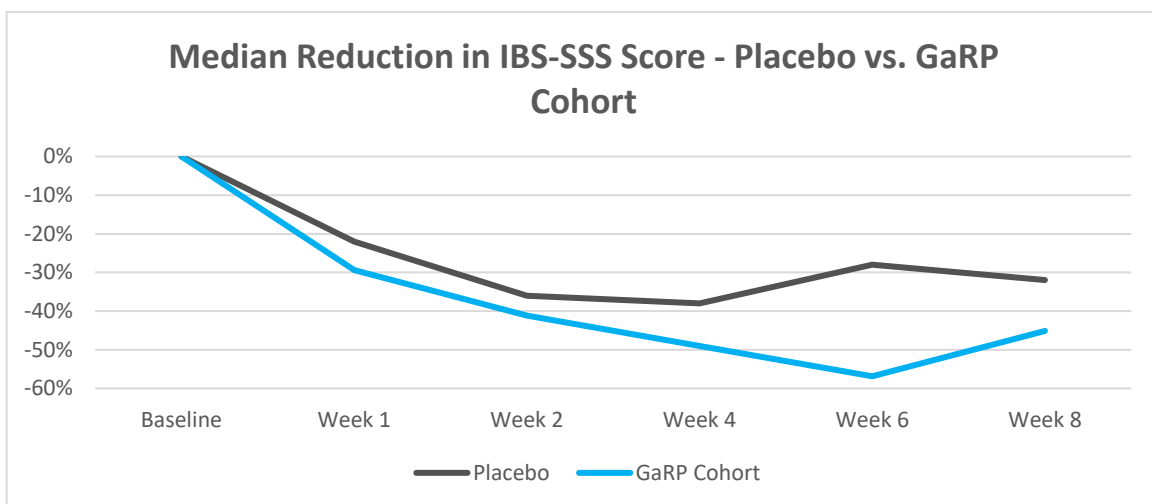
Headline analysis was of the primary endpoints of safety, including treatment related adverse events, and the IBS-SSS (“SSS” being Severity Scoring System) reduction compared to placebo. Secondary endpoints analysed included Adequate Relief (AR-IBS), Anxiety within the well-known HADS (Hospital Anxiety & Depression Scale ) and improvement in IBS-SSS compared to baseline.

Anatara met with the DSMB (Data Safety Monitoring Board) for the GaRP-IBS trial on the 15<sup>th</sup> April 2025. The DSMB confirmed the Company’s interpretation that the analysis revealed no concerning safety signals and that the product was well tolerated. The Company notes the value of obtaining safety data, especially from a cohort of 78 participants assigned to the GaRP product treatment arms in a randomised, placebo-controlled, double-blind trial.

Anatara’s Executive Chair Dr David Brookes commented: “Not reaching significance for the primary efficacy endpoint in any quality trial has to be a real disappointment for all involved, as it is the common goal, however the trial has still delivered significant findings. While taking the opportunity to again thank participants and those involved in conducting the trial, it is important to consider the positive information and results obtained that can still be both clinically and commercially relevant. The GaRP product appears to outperform placebo for IBS-SSS reduction but does not reach statistical significance, and the secondary endpoints suggest broader benefits consistent with the hypothesis on the mechanism of action. In particular, the statistically significant improvement in mild background anxiety points to support for the benefits to the gut-brain axis through assisting the homeostasis of the microbiome dynamics. Anatara will work efficiently towards summarising the pre-clinical studies and the IBS trial findings for commercial discussions. We will be endeavouring to maximise the value of the GaRP project while progressing the anti-obesity project concept, and there is already a focus on other opportunities and future directions. “

## Headline Data Overview

The first graph demonstrates the anticipated strong placebo effect in the first 2 weeks. The mean reduction in the IBS-SSS appeared to be approaching significance before the Week 8 with the GaRP cohort having a greater improvement in symptoms. Week 8 is the last week of participants taking either the randomised placebo or product and the scoring from the cohort arms converge at the end of this week. An improvement in IBS-SSS of more than 100 points is sustained.



The table below details the median IBS-SSS Scores from the modified-ITT (Intent-To-Treat) trial group that highlight the positive change in patients' IBS scores on the GaRP Cohort. A 45% reduction in an IBS Score translates to a significant positive change in day-to-day life, a benefit that cannot be understated. An IBS-SSS score of 255 being towards the high end of moderate IBS compared with a score of 140 in the mild IBS category.

\*(IBS-SSS 0-500 gradings: 75-175 Mild; 175-300 Moderate; over 300 Severe)

Median IBS-SSS Score – Baseline to week 8		
	Placebo	GaRP Cohort
	n=51	n=48
Baseline	250	255
Week 1	195	180
Week 2	160	150
Week 4	155	130
Week 6	180	110
Week 8	170	140
Difference baseline score to week 6 score	-70	-145
%	-28%	-57%
Difference baseline score to week 8 score	-80	-115
%	-32%	-45%

### Explanation of Secondary Endpoint – Hospital Anxiety & Depression Score (HADS)

Hospital Anxiety and Depression Scale (HADS) is a 14-item self-reported measure that was specifically developed to assess anxiety and depression in people with medical illnesses. It has two subscales, which evaluate anxiety and depression.

Scoring: (for Depression and anxiety):

- 0-7 = Normal
- 8-10 = Borderline abnormal (borderline case)
- 11-21 = Abnormal (case)

### Secondary Endpoint – Hospital Anxiety & Depression Score (HADS) Tables

The next graphs show the statistically significant improvement in background anxiety scores, which is incorporated in the combined HADS score. Depression scores remain in the normal range and hence the conclusion is that there is no adverse emotional effect with the benefit of improving mild background anxiety for those participants on GaRP. This is encouraging data and consistent with the mechanism of action of the GaRP product being designed to assist repair and maintenance of the gastrointestinal tract as a barrier, as well as the homeostasis and dynamics of microbiome.



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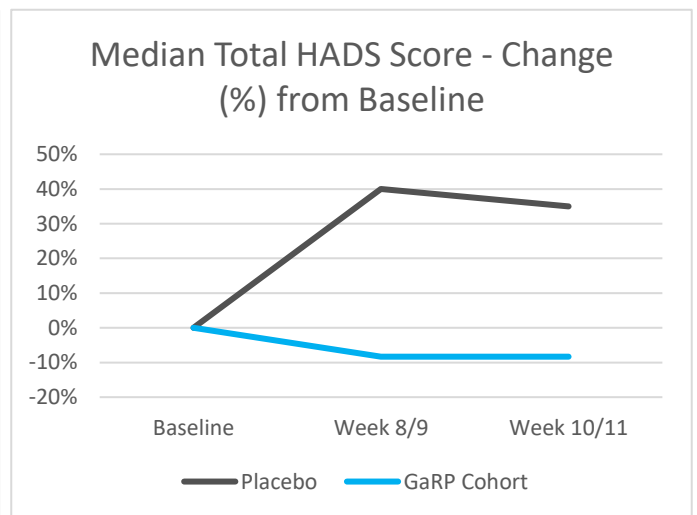
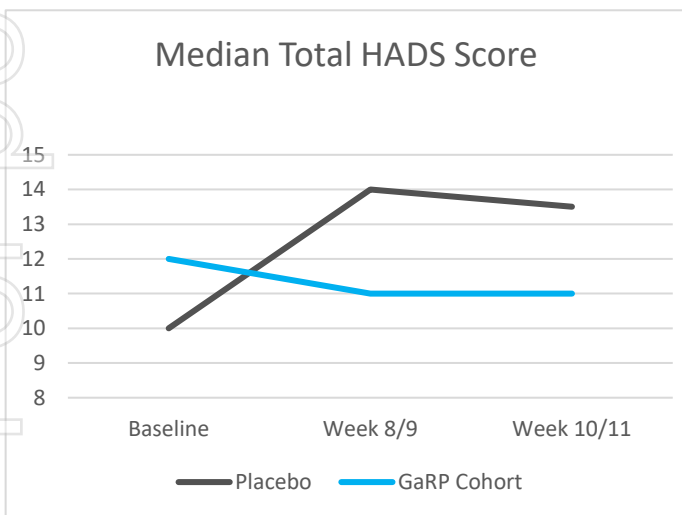
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Median Total HADS Score – Baseline to week 10/11		
	Placebo	GaRP Cohort
	n=56	n=57
Baseline	10	12
Week 8/9	14	11
Week 10/11	13.5	11
<b>Change from Baseline</b>	<b>3.5</b>	<b>-1</b>
<b>Change from Placebo</b>		<b>(P=0.014)</b>

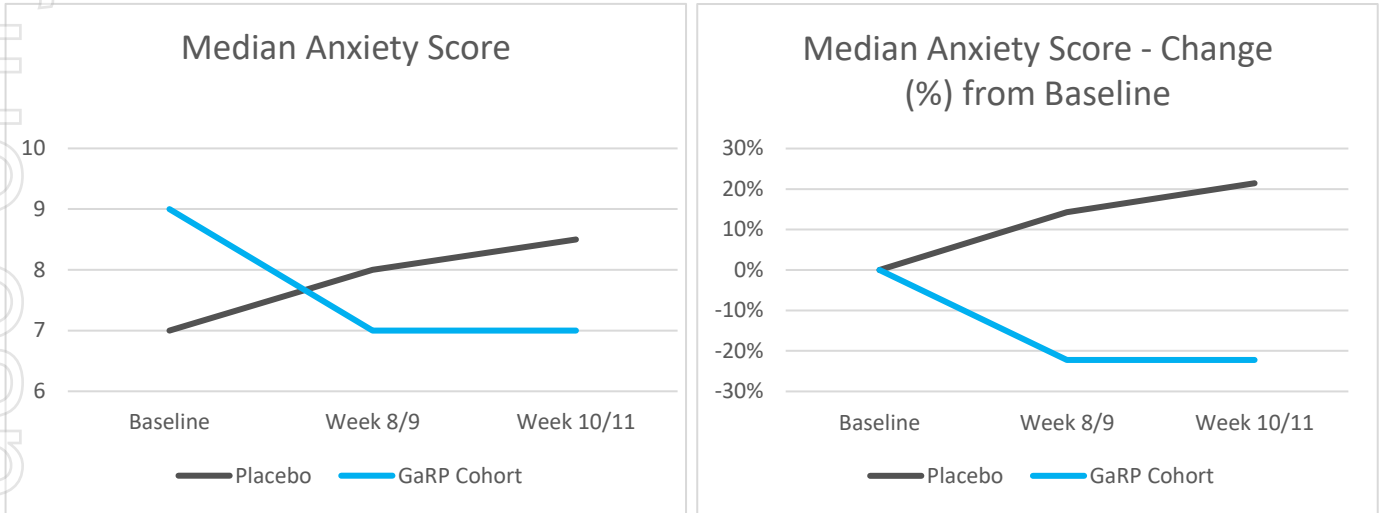
Median Total Anxiety Score – Baseline to week 10/11		
	Placebo	GaRP Cohort
	n=56	n=57
Baseline	7	9
Week 8/9	8	7
Week 10/11	8.5	7
<b>Change from Baseline</b>	<b>1.5</b>	<b>-2</b>
<b>Change from Placebo</b>		<b>(P=0.024)</b>

### Total Hospital Anxiety & Depression Score (HADS)

Baseline to week 10/11



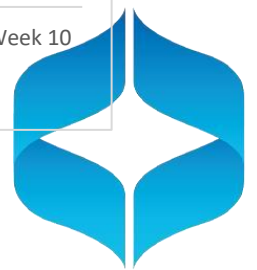
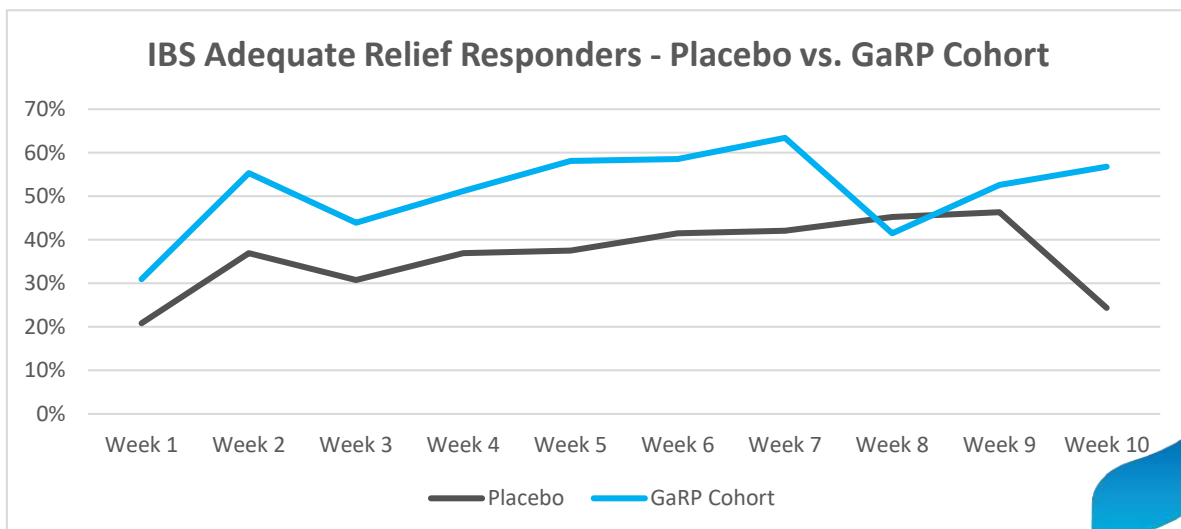
## Anxiety Scores Baseline to week 10/11



## Adequate Relief for IBS Overview

The Adequate Relief for IBS (AR-IBS) graph highlights many of the observations and interpretation dilemmas. Again, there is separation with the GaRP cohort performance superior until the end of Week 8, in which the participants know it is the last week of observational recording while randomised to either the placebo or the GaRP treatment. There are no biomarkers for objective assessment of IBS disease activity and the scoring systems are subjective and drawn out. (i.e. AR-IBS simply answer, do you feel better or improved on what you are taking?)

The “Adequate Relief Responders” graph demonstrates the convergence seen in IBS-SSS at Week 8 and then an apparent sustained benefit that is statistically highly significant. By Week 10, which is 2 weeks on from having ceased taking the product or placebo, the active treatment GaRP cohort arm maintains a perception of having had an “adequate response” that is statistically highly significant versus placebo. This can be extrapolated to support the GaRP mechanism of action of restoring and maintaining the gastrointestinal tract lining as a barrier and the homeostasis of the microbiome dynamics, thereby maintaining a response post-treatment.



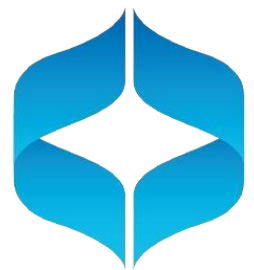
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Placebo and GaRP Cohort Responders Table

Responders – Week 1 to week 10		
	Placebo	GaRP Cohort
Week 1	21%	31%
Week 2	37%	55%
Week 3	31%	44%
Week 4	37%	51%
Week 5	38%	58%
Week 6	41%	59%
Week 7	42%	63%
Week 8	45%	41%
Week 9	46%	53%
Week 10	24%	57%
Difference week 1 score to week 8 score	24%	11%
%	117%	34%
Difference week 1 score to week 10 score	3%	26%
%	17%	83%

Stage 2 of the GaRP-IBS trial was the planned extension of the Phase II trial that followed the successful completion of Stage 1 which reported on 20 patients with a greater than a 50% reduction in IBS symptoms and with safety profile confirmed. Stage 2 was hoped to confirm the highly encouraging and clinically meaningful interim results from Stage 1 of the GaRP-IBS clinical trial which created partnering interest.

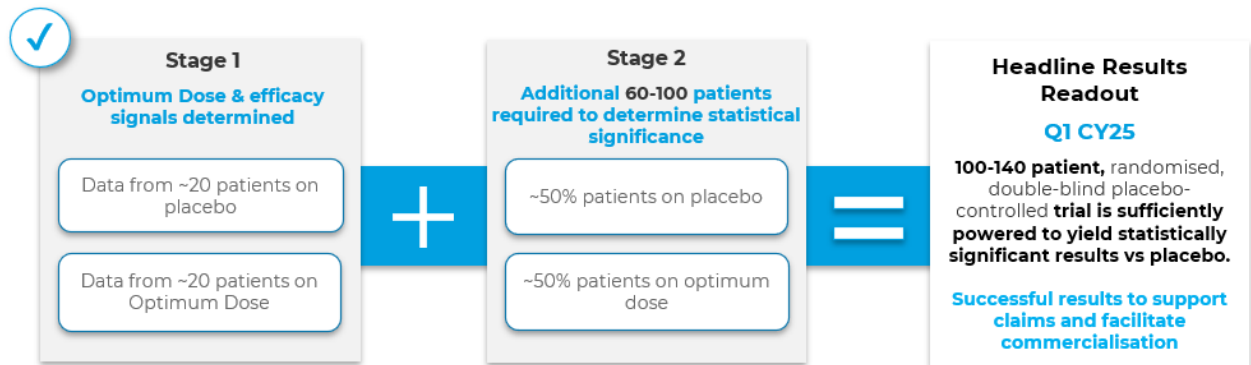
On the 14<sup>th</sup> January in the Quarterly Activities Report, the Company announced the Stage 2 enrolment number in the GaRP-IBS trial being confirmed as 71 Intent-To-Treat (ITT) participants. The trial participant numbers were in line with Company expectations, even after determining a fully assessable modified-ITT data set of 62 participants for IBS-SSS after taking into consideration those with an unacceptably low IBS-SSS at baseline. Hence, the Company analysed both the full ITT group and a modified-ITT that only included participants in the trial with a baseline IBS-SSS score equal to or greater than 150 at the commencement of trial involvement. The trial protocol had the IBS-SSS parameters of 175-350 in screening for eligibility to participate in the trial process. Anatara intends to review data from the trial across a number of participant subsets, including criteria such as IBS-D (Diarrhoeal only) versus IBS-M (mixed diarrhoea and constipation). This will further our understanding of the results and potential for the product.



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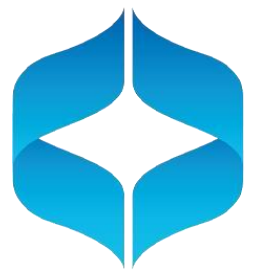
The data from both Stages of the trial formed the basis of the completed data for the final analysis. The sub-groups of participants from Stage 1 are included with eligible participants from Stage 2 for the final analysis, which resulted in a total of approximately 100 participants in the modified-ITT analysis. The trial was intended to be sufficiently powered to deliver statistically significant results versus placebo. (Please see further detail on the Trial Design and GaRP below)

## GaRP-IBS Clinical Trial Design



## About GaRP

Anatara's GaRP product is a multi-component, multi-coated complementary medicine designed to address underlying factors associated with chronic gastrointestinal conditions such as IBS and IBD. GaRP is the working name for the product from the Company's Gastrointestinal ReProgramming project that was designed to assist restoration and maintenance of the gastrointestinal tract (GIT) lining as a barrier and assist the homeostasis of the microbiome. The product is made of GRAS (Generally Regarded As Safe) components.



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## Progress of Anti-Obesity Project

The planned *in-vivo* pre-clinical experiments, that have ethics approval, are underway with the University of Newcastle, as previously advised. The initial studies are anticipated to take approximately 6 months through to completion, depending on the observations of markers and weight control in the initial animal (mice) studies. The study length with the need for further mice cohorts will be determined on scientific outcomes and milestones, and these may extend the overall study a further few months.

The anti-obesity project has been designed to develop an oral medication to assist weight reduction and sustaining weight control in conjunction with other contemporary treatments and approaches. Specifically, the product is being developed with the target of assisting the maintenance of weight loss and limiting rebound weight gain following cessation of contemporary weight loss medications.

While the Company needs to protect the project at this early stage, the mechanism of action involves the stimulation of endogenous GLP-1. The Company will assess several compounds of interest (that have been sourced/manufactured) in the pre-clinical studies to determine the best candidate/s going forward. The candidate compounds selected have been shown to target the same biochemical mechanism that is the focus of the Proof-of-Concept (POC). The dosage regimes have been predicted from published pre-clinical and clinical studies. The Company has allocated more than \$250,000 to the POC studies for the anti-obesity project and will determine further steps as the results of these initial studies are assessed.

## Corporate and business changes

While committed to the Anti-Obesity Project Proof of Concept studies, the Company is assessing other opportunities and directions. The summarisation of the GaRP project pre-clinical and clinical work remains a priority to enhance the understanding of the commercial possibilities for the GaRP product in gastrointestinal health. The patent position for the GaRP project is current and remains protected. The Company is still of the view that the product has the potential for broad indications, including in the management of a healthy gut-brain axis. However, manufacturing and the procurement of ingredient components are not a priority. Furthermore, only essential roles will be maintained around the retracted activities until the Company's direction is further defined.

Mr. John Michailidis will be in a non-executive director role only from the end of this week as part of a planned transition to retire the COO role to coincide with Company inflection points. Mr. Simon Erskine will reduce his workload next month to 0.8 FTE as CDO for the foreseeable future. These operational initiatives accompany general reduction in contracted services to the Company that are not immediately relevant following the GaRP-IBS trial outcome.

The Company's cash position is stable and the accumulating R&D tax incentive rebate was approximately \$500k at the end of H1CY25.



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**About Anatara Lifesciences Ltd**

Anatara Lifesciences Ltd (ASX:ANR) is developing and commercialising innovative, evidence-based health products where there is significant unmet need. Anatara is focused on building a pipeline of human health products with a particular focus on conditions that involve the complexity of the gastrointestinal tract. Underlying this product development program is our commitment to delivering real outcomes for patients and strong value for our shareholders.

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