ASX Release

Anatara Lifesciences 4C & Q1 FY24 Activities Report

Q1FY 2024 Highlights

- Finalised Stage I of Irritable Bowel Syndrome (IBS) trial of "GaRP" & announced positive outcomes from Interim Analysis (ASX: 28 September 2023)
- Interim analysis confirmed primary endpoints of safety and efficacy trend in the IBS-SSS with Low Dose selected for Stage 2
- Subsequently announced (ASX: 17 October 2023) positive analysis of secondary endpoints of Hospital Anxiety and Depression (HADS) and Quality of Life (QOL) with marked improvement in the Low Dose cohort
- Received R&D tax refund of $0.923m in August 2023
- Continuation of appraisal of other opportunities for the Company in healthcare

ADELAIDE, 31 October 2023: Anatara Lifesciences (ASX: ANR or "the Company"), a developer of evidence-based solutions for gastrointestinal diseases in humans and animals, is pleased to provide a general Company update including the progress of the Gastrointestinal ReProgramming (GaRP) trial for IBS.

GaRP – Irritable Bowel Syndrome (IBS) - Phase II Trial Update

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 is made of GRAS (Generally Regarded As Safe) components and is designed to assist restoration and maintenance of the GIT lining and the homeostasis of the microbiome.

As announced on the 28th September, 2023, 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.

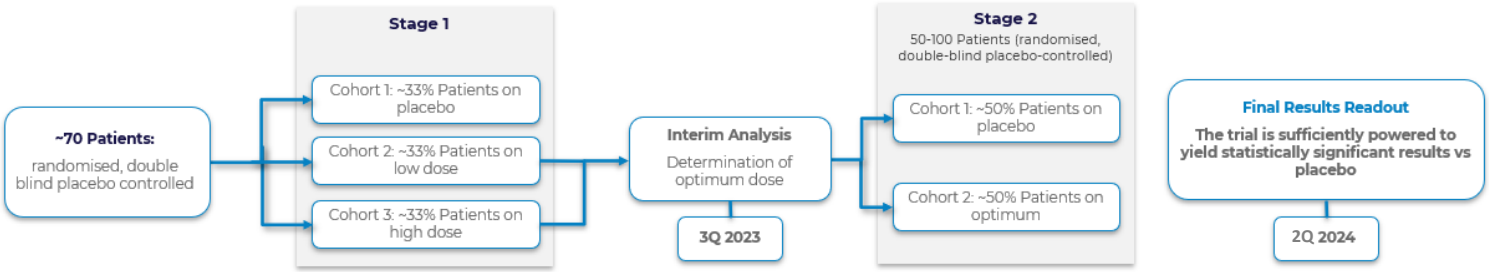
Subsequently, the Company announced in October 2023 a positive analysis of the secondary endpoints of Quality of Life (QoL) and the Hospital Anxiety and depression Score (HADS). The improvement of the

QoL scores was anticipated to reflect the trend of improvement in the primary endpoint of IBS-SSS. Analysis of improvement in HADS revealed highly significant improvement in anxiety and depression scores on Low Dose ($p < 0.05$) for the overall treatment. The Company considered this a remarkable result while cautioning on the low numbers involved at this stage of the full trial.

Stage 2 design of the trial is to confirm/establish statistical significance for primary and secondary endpoints through greater numbers. Anatara is now preparing for Stage 2 of the GaRP trial.

The analysis of these GaRP-IBS trial Stage 1 secondary endpoints furthers a belief that GaRP as a complementary medicine with rejuvenating gastrointestinal tract (GIT) effects will provide relief for sufferers of non-specific GIT symptoms and be an important adjunctive therapy in mainstream medical indications, such as IBS and IBD (Inflammatory Bowel Disease. Furthermore, the Company is very encouraged by the results supporting the method of action (MOA) for GaRP as a product designed with the potential to improve quality of life for patients with gastrointestinal disorders (GIT) by influencing the complexities of the gut-brain axis through restoration and maintenance of the integrity of the GIT lining and assisting the homeostasis of the microbiome.

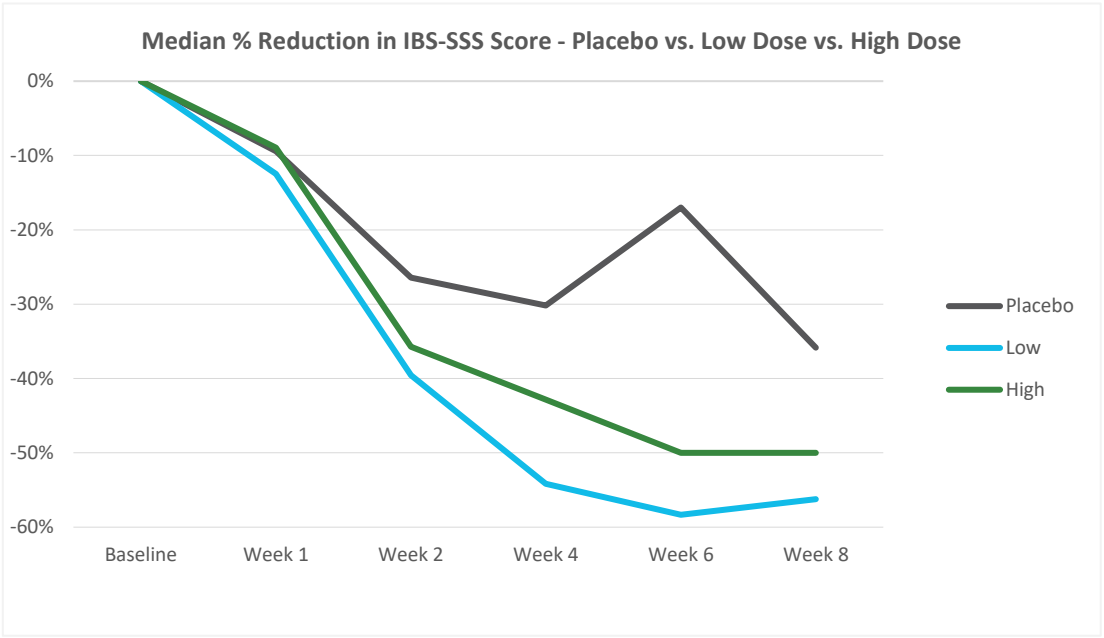
GaRP-IBS Clinical Trial Design



Headline Data Overview – Stage 1 (Previously Reported to ASX 28/09/2023)

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 deliver statistically significant endpoints. 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[1].

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.

Secondary Endpoint Data – Stage 1

The analysis of the secondary endpoints of the change from baseline in the Hospital Anxiety and Depression Score (HADS) and the change in the Quality of Life for Irritable Bowel Syndrome sufferers (IBS QoL) showed marked improvement for patients on the Stage 1 Low Dose.

Secondary Endpoint – Hospital Anxiety & Depression Score (HADS)

The HADS reduction was highly significant for the Low Dose cohort across anxiety and depression ($p < 0.001$) versus placebo with a reduction of 6 points. This result is also clinically meaningful.

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.

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

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 Showing Mean Scores*

TOTAL SCORE – Hospital Anxiety & Depression Score (HADS)			
	Placebo	**Low Dose**	High Dose
	N=20	**N=20**	N=21
Baseline	11.6	**13.3**	14.2
Week 8/9	14	**9.6**	13.9
Week 10/11	13.5	**9.2**	15.2
Change from Baseline	3.5	-4.0	-0.7
Versus Placebo		**-6.0 (P<0.001)**	-2.4

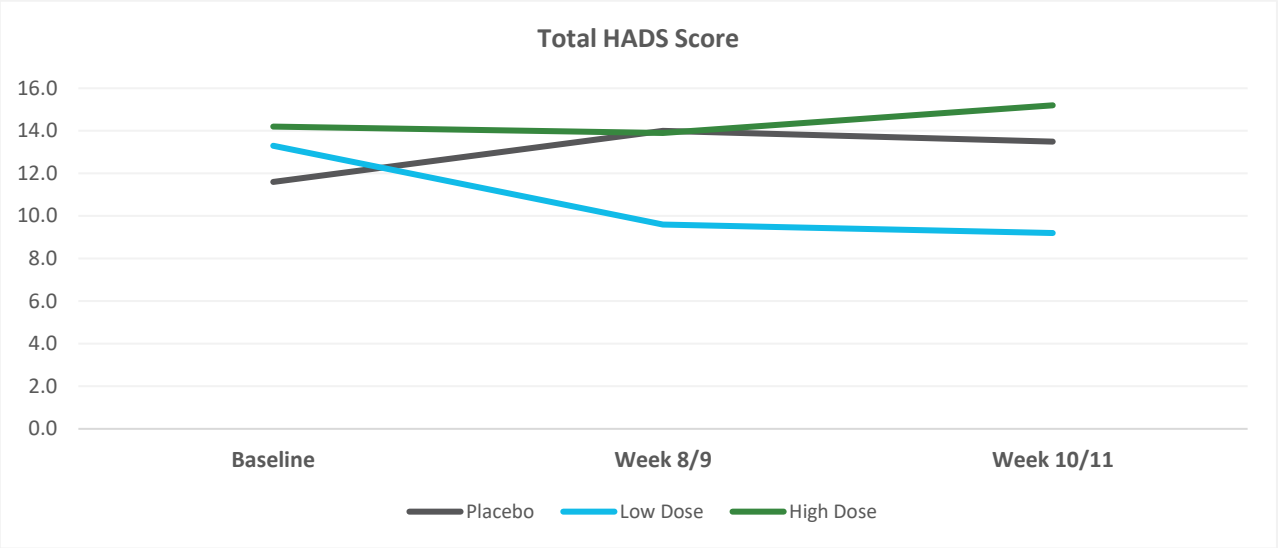
ANXIETY SCORE – Hospital Anxiety & Depression Score (HADS)			
	Placebo	**Low Dose**	High Dose
	N=20	**N=20**	N=21
Baseline	7.9	**9.1**	8.5
Week 8/9	9.2	**6.4**	8
Week 10/11	9	**6.3**	8.7
Change from Baseline	2.0	-3.0	-0.5
Versus Placebo		**-3.7 (P<0.001)**	-1.6

DEPRESSION SCORE – Hospital Anxiety & Depression Score (HADS)			
	Placebo	**Low Dose**	High Dose
	N=20	**N=20**	N=21
Baseline	3.7	**4.2**	5.7
Week 8/9	4.8	**3.1**	5.9
Week 10/11	4.5	**2.8**	6.5
Change from Baseline	1.5	-1.0	-0.2
Versus Placebo		**-2.1 (P=0.033)**	-0.7

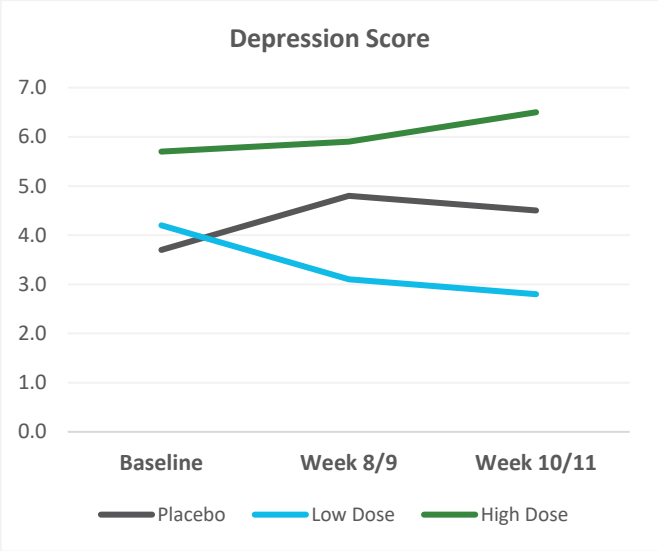
*Statistical analysis of Mean scores accounted for missing data so that the non-missing value did not contribute to the mean difference change from baseline or the difference between means of treatment versus placebo. Statistical analysis conducted by an independent third party.

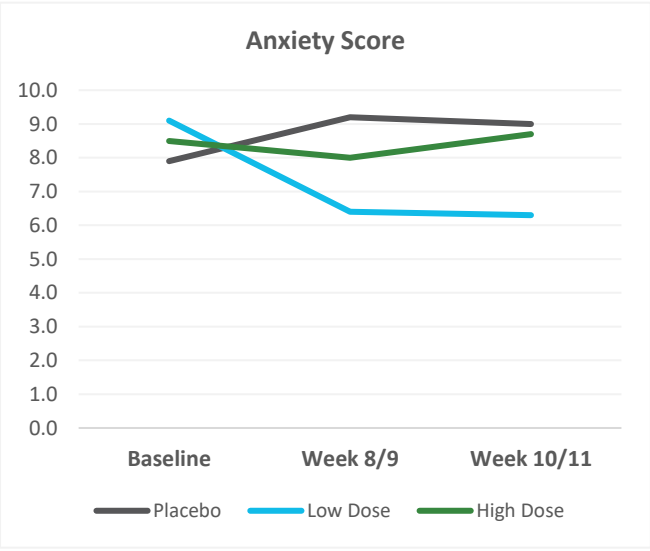
Total Hospital Anxiety & Depression Score (HADS)

Baseline to week 10/11



Depression and Anxiety Scores Baseline to week 10/11





Secondary Endpoint – IBS Quality of Life Score

IBS quality of life (IBS-QOL):

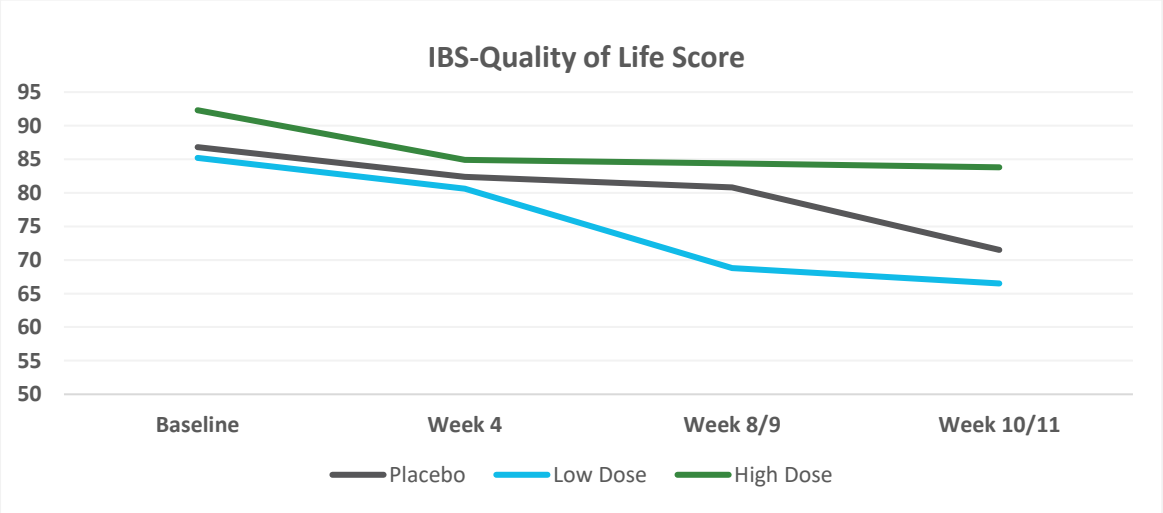
The IBS-QoL is a 34-item questionnaire that assesses the degree to which IBS interfered with quality of life for a subject over the past 30 days. Each item is rated on a 1 to 5 Likert scale, with higher values indicating a lower quality of life. Scores are summed to comprise eight subscales including a total score

with a range of 34 to 170. **A decrease of 10 points or more is considered a clinically meaningful improvement.**

- The Secondary Endpoint data for the IBS QoL showed a strong trend of improvement between the Low Dose and Placebo group from Baseline to:
  - week 8/9 of 11.4 (p=0.10)
  - week 10/11 of 8.3
- The higher placebo score at week 10/11 can be partly explained by difficulties for patients on placebo remaining in the trial for the full duration. Patients suffering from difficult to manage symptoms tend 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.

IBS-Quality of Life Score			
	Placebo	**Low Dose**	High Dose
	N=20	**N=20**	N=20
Baseline	86.8	**85.2**	92.3
Week 4	82.4	**80.6**	84.9
Week 8/9	80.8	**68.8**	84.4
Week 10/11	71.5	**66.5**	83.8
Week 8/9 - Change from Baseline	-3.1	**-14.6**	-11.4
Week 8/9 - Versus Placebo		**-11.4 (P=0.10)**	-6.2
Week 10/11 - Change from Baseline	-6.0	**-10.2**	-14.5
Week 10/11 - Versus Placebo		**-8.3 (P=0.29)**	-8.4

*Statistical analysis of Mean scores accounted for missing data so that the non-missing value did not contribute to the mean difference change from baseline or the difference between means of treatment versus placebo. Statistical analysis conducted by an independent third party.



Depending on the diagnostic criteria employed, IBS affects around 11% of the population globally. Around 30% of people who experience the symptoms of IBS will consult physicians for their IBS symptoms. These IBS sufferers do not have significantly different abdominal symptoms to those who do not consult, but generally have greater levels of anxiety and a lower quality of life. Internationally,

there is a female predominance in the prevalence of IBS. The age group tends to be younger adults with the incidence of IBS 25% less in those over 50 years and there is no association with socioeconomic status[2].

The Anatara GaRP-IBS trial recruited patients with scores in the 175-350 range on the IBS-SSS which highlights that this trial only included patients with moderate to severe IBS symptoms who often present with higher-than-normal levels of anxiety and depression.

The Company notes it is very impressive, albeit in small numbers, to not only reduce patients' IBS symptoms but also to improve comorbidities, such as anxiety and depression. Being able to make verified statements about improving clinically significant symptoms of anxiety and depression increases the commercial potential for the GaRP product in a global market, as there are simply not many products that address the spectrum of life altering related suffering associated with these complex GIT disorders.

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 the GaRP 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.

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

[2]https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3921083/#:~:text=Depending%20on%20the%20diagnostic%20criteria,physicians%20for%20their%20IBS%20symptoms.

Ongoing corporate initiatives

Following the GaRP interim trial results, Anatara continues to engage with global pharma companies interested in expanding their portfolio of complementary medicines. The trial is garnering interest from global leaders in the GI field due to the strong evidence-based design of the GaRP trial.

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. There are also ongoing discussions for potential uses of Anatara's established products and know-how for animal health indications.

Summary Q1 FY2024 cashflows

The Company's cash at the end of the quarter was $0.537 million (30th June 2023: $0.351 million). Net cash from operating activities during the quarter was $0.185 million, compared to a $0.826 million cash outflow from operating activities in the previous quarter.

This was driven primarily by the application for the 2023 Research & Development Tax Rebate, resulting in a refund of $0.923 million in August. All expenditure was as anticipated as Stage 1 of the GaRP trial was finalised and the Interim Analysis conducted.

The aggregate payments to related parties and their associates during the quarter totalled $69,000, which includes directors' fees and superannuation.

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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.

those documents and all of those losses and damages are expressly disclaimed. Any opinions expressed reflect the Company's position at the date of this presentation and are subject to change.

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Appendix 4C

Quarterly cash flow report for entities subject to Listing Rule 4.7B

Name of entity

Anatara Lifesciences Ltd (ASX:ANR)

ABN	**Quarter ended ("current quarter")**
41 145 239 872	30 September 2023

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (3 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	-
1.2	Payments for		
	(a) research and development	(315)	(315)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(23)	(23)
	(d) leased assets	-	-
	(e) staff costs	(157)	(157)
	(f) administration and corporate costs	(316)	(316)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	-	-
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	923	923
1.8	Other (provide details if material)	73	73
1.9	**Net cash from / (used in) operating activities**	**185**	**185**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (3 months) $A'000
2.2	Proceeds from disposal of:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-
2.3	Cash flows from loans to other entities	-	-
2.4	Dividends received (see note 3)	-	-
2.5	Other (provide details if material)	-	-
2.6	**Net cash from / (used in) investing activities**	**-**	**-**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	-
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	-	-
3.4	Transaction costs related to issues of equity securities or convertible debt securities	-	-
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (provide details if material)	-	-
3.10	**Net cash from / (used in) financing activities**	**-**	**-**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	351	351
4.2	Net cash from / (used in) operating activities (item 1.9 above)	185	185
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (3 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	-	-
4.5	Effect of movement in exchange rates on cash held	-	-
4.6	**Cash and cash equivalents at end of period**	**537**	**537**

5.	Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	Current quarter $A'000	Previous quarter $A'000
5.1	Bank balances	537	351
5.2	Call deposits	-	-
5.3	Bank overdrafts	-	-
5.4	Other (provide details)	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**537**	**351**

6.	Payments to related parties of the entity and their associates	Current quarter $A'000
6.1	Aggregate amount of payments to related parties and their associates included in item 1	69
6.2	Aggregate amount of payments to related parties and their associates included in item 2	

Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an explanation for, such payments.

Item 6.1 Reflects amounts paid to directors including director's fees, salaries, superannuation, bonuses and consulting fees (excluding reimbursements).

7.	**Financing facilities** *Note: the term "facility' includes all forms of financing arrangements available to the entity.* *Add notes as necessary for an understanding of the sources of finance available to the entity.*	**Total facility amount at quarter end $A'000**	**Amount drawn at quarter end $A'000**
7.1	Loan facilities	-	-
7.2	Credit standby arrangements	-	-
7.3	Other (please specify)	-	-
7.4	**Total financing facilities**	-	-

7.5	**Unused financing facilities available at quarter end**	-

7.6 Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.

8.	**Estimated cash available for future operating activities**	**$A'000**
8.1	Net cash from / (used in) operating activities (item 1.9)	185
8.2	Cash and cash equivalents at quarter end (item 4.6)	537
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	537

8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	N/A

Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a figure for the estimated quarters of funding available must be included in item 8.5.

8.6 If item 8.5 is less than 2 quarters, please provide answers to the following questions:

8.6.1 Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?

Answer: N/A

8.6.2 Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?

Answer: N/A

8.6.3 Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?

Answer: N/A

Note: where item 8.5 is less than 2 quarters, all of questions 8.6.1, 8.6.2 and 8.6.3 above must be answered.

Compliance statement

1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.

2 This statement gives a true and fair view of the matters disclosed.

31 October 2023

Date: .....

Full Board / David Brookes – Chairman

Authorised by: .....
(Name of body or officer authorising release – see note 4)

Notes

1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.

2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.

3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.

4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [*name of board committee – eg Audit and Risk Committee*]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".

5. If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.