Key Messaging and General Script for Clinical Study Teleconference

Overall Key Messages:

- Medibio is a health technology company that has completed or participated in many reviews and studies
- The morphology of Medibio has evolved since the company was founded on a clinical hypothesis 15 years ago. The rigorous FDA trial we just completed is an important step in our work
- The 70% accuracy differs from previous communications that estimated 85%:
    - Greater number of patients delivers greater statistical power, however it may require rigorous study methodology
    - The study targeted general population in a normal-daily-home environment
- Global study confirms Medibio's Depression Diagnostic Aide (DX04)
- With 70% accuracy, 70% sensitivity and 71% specificity these results demonstrate utility in long-term monitoring
- Study results support the FDA DeNovo submission
- Diagnostic algorithm is designed to provide mental health practitioners with an objective technology to aide in assessment of depression

General Script:

Peter Taylor To Introduce Brian Mower:
Peter: Welcome. Thanks for joining the call. I am going to kick things off by introducing Brian Mower, Chief Financial Officer and Interim Chief Executive Officer for Medibio. Brian has 22 years experience in senior financial leadership, including the last 19 years in successfully commercializing innovative medical device technologies.

Brian: Thank you, Peter. Welcome everyone and thank you for joining us today. On behalf of all Medibio staff and board members, we appreciate your continued investment, the support of our company and interest in our technology. The purpose of today's call is to discuss last week's announcement of our FDA clinical study results.

The results showed statistical accuracy of the algorithm to detect a major depressive episode and is a milestone achievement in the company's development of an objective test for aiding in the diagnosis of depression in patient care.

This study is a result of lots of hard work, effort, and investment. Many thanks to the internal team, our clinical study partners, the study participants, and the external consultants that helped us thru this process. I am humbled by the efforts of all involved and grateful for their work. Having been involved with medical device technologies and various FDA submission for nearly 20 years, I felt it was important to provide additional education to the marketplace on these clinical study results.

I'm grateful to have each of the participants on the call with me. They are an impressive group. Together we have a combined nearly 150 years of experience in respective areas. I'd like to take a few minutes to introduce the other participants on the call:

Archie Defillo, the Chief Medical Officer at Medibio. Archie is a neurosurgeon by education and practice, has over 25 years of clinical experience with neurological diseases, and for the

past 13 years his efforts have been focused in neurological research. Based on his extensive academic work, in 2012, he was selected a scientific member of the Congress of Neurological Surgeons.

Dr. Franklyn Prendergast serves on the Medibio Board of Directors and chairs the Medibio Scientific Advisory Board. He is a Rhodes Scholar from Oxford University and earned a doctorate degree in biochemistry. He has held many leadership positions at Mayo Clinic, including Chair of the biochemistry department, Director of Research, Board of Governors, and Board of Trustees. He has also been recognized as a Mayo Distinguished Investigator and has held numerous appointments with industry groups such as National Cancer Institute and National Institute of Health.

Dr. Marie Olseth is a Medibio Scientific Advisory Board member, and for over 20 years has been in private practice as a Board Certified Adult Psychiatrist. She earned her doctor of medicine degree from the University of Minnesota Medical School. She is a member of the American Psychiatric Association, the Minnesota Psychiatric Society, the American Medical Association, and the Minnesota Medical Association. She has a Minnesota Medical License, a Wisconsin Medical License, and is certified by the American Board of Psychiatry.

Amy Fowler (RAC, JD) brings over 25 years of experience guiding medical devices and pharmaceuticals to market. She counsels clients on regulatory strategies, is well versed in FDA process, and prepares various FDA filings, including Pre-Submission, 510(k), DeNovo, IDE, IND, DMF, and NDA submissions. Her client projects include software devices, dental products, wound dressings, apps and combination products. Amy also serves as an expert for US and EU UDI issues. Amy is a former Chair of the Minnesota State Bar Association Food, Drug, and Device Section. She has a Juris Doctorate in law and Bachelor of Chemistry. As our regulatory legal counsel, Amy has assisted Medibio in working with the FDA on our DeNovo submission.

Dr. Melissa Martinson (MS, PhD) is a health services researcher and biostatistician, and is Adjunct Associate Professor in the Division of Health Policy and Management, School of Public Health, University of Minnesota. Her commercial experience includes 20 years of clinical trials, health economics, and outcomes studies in both medical device and pharmaceutical companies. She is President of Technomics Research, where she focuses on research and statistics and is an integral part of the validation process for our clinical study.

We have very good people involved with this Company. Experts in their fields, and I want you to hear from these experts as they address your questions.

Peter: Archie will start us off with some overview comments. And we have received a number of questions from investors that our participants will address. I'll read the question and then turn it over to an expert for the answer:

Color coded for each participant: Archie Melissa Amy Franklyn Marie

Archie: The current study and results were published in accordance with FDA Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Test. The FDA works with companies on clinical study design and results to support successful completion. The

FDA allows alternative approaches, as long as those approaches are based on scientific evidence and supported by regulatory requirements. The DXO4 study is viable for the company moving forward as support for the current FDA DeNovo application.

The FDA recognizes two major benchmark categories for assessing diagnostic performance and accuracy of a new diagnostic device. These categories are 1) comparison to a reference standard, and 2) comparison to a predicate. As you are all aware, we filed a DeNovo application as there isn't a predicate to our technology, so our diagnostic accuracy must be compared to a reference standard.

By definition, the DXO4 reference standard for reporting accuracy, sensitivity, and specificity derives from physicians inter-rater reliability, and current subjective evaluations. However, those evaluations could introduce **verification bias** within a research protocol.

According to FDA requirements there are different ways to describe diagnostic accuracy. Appropriate measures include estimates of sensitivity and specificity pairs, likelihood ratios of positive and negative results,this normally applies to case-control studies. When using a cross-sectional study design, like the DOX4, positive and negative predictive values can be also calculated.

The DX04 study and design is not perfect. We are working with the FDA to reach a common path to demonstrate clinical significance.

1-Why is this study positive? Why is this version of the study better than ones before?

Frank: There are differences between each study. You cannot compare results from these studies against each other because it is like comparing apples and oranges. When conducting research, you start with a hypothesis then gather your data and then analyze it compared to the hypothesis. If each study has a unique hypothesis and conducted under different conditions, then it is absolutely impossible to compare the results. I commend Medibio for continually improving the study hypothesis. This company started with just an idea, then moved into studying that idea in various manners, each opportunity building upon the ones before, and now it has completed a rigorous FDA study that has good results. Bravo to the Medibio team.

Archie: Each prior study provided a unique understanding of our technology. We built a set of foundational knowledge from those studies. However, prior studies lacked strong methodology and statistical power to make any definitive statement. The DX03 study reported in August 2017 was a pilot study. The DX04 study is a confirmatory validation study. Two different research methodologies.

The DX04 validation required more rigor, sophistication, and definition around the protocol and performance than previous studies. Our hypothesis test, although calculated at the time, was higher than used previously, the number of study participants was greater, and the data results were reviewed in a blinded manner. Within the current submission, The FDA is not likely to accept data from any preceding study, other than the DX04, because of the conditions that data it was collected under.

2-What is DeNovo?

Amy: The Medibio Depressive Diagnostic Aide (DDA) is an innovative device for which no predicate device exists in the FDA classification database. Entirely new devices such as the DDA are submitted using the "de novo" process. Medibio engaged the FDA pre-submission process to verify the "novel" nature of the DDA and that no existing classification or predicate device on the market. An approved DeNovo would result in an entirely new product code and regulation. This product code would then serve as a predicate device for future Medibio products.

Several types of premarket submissions can be made to FDA. In order to legally market a device in the US, the most common forms of premarket submissions to FDA are the 510(k) premarket notification submission and the PMA premarket approval. Another lesser known premarket submission is the de novo submission.

A 510(k) is a premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective (substantially equivalent) to a legally marketed device that is not subject to PMA.

Premarket approval (PMA) is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices, and the most stringent of the device marketing applications.

The de novo pathway for device marketing rights was added to address novel devices of low to moderate risk that do not have a valid predicate device. Upon successful review of a de novo submission, FDA creates a classification for the device, a regulation if necessary, and identifies any special controls required for future premarket submissions of substantially equivalent devices.

3-What is the medical claim you are seeking from the FDA?
Amy: These are the Intended Use and Indications for Use statements we have used in our FDA communications:

Intended Use: The Medibio Depression Diagnostic Algorithm is used by physicians familiar with physiology, diagnosis, and treatment of mental health disorders and who have an understanding of the principles, clinical applications, and risks associated with characterizing heart rate, activity, and supine rest patterns and diagnosis of major depressive disorder.

The Medibio Depression Diagnostic Algorithm is used when an individual is suspected to have moderate to severe depression. The Medibio Depression Diagnostic Algorithm will generally be used once per episode of suspected depression but may be used multiple time should multiple episodes present.

The Medibio Depression Diagnostic Algorithm is intended for prescription use only, by or on the order of a physician. The primary target population is moderately-to-severely depressed patients that are being diagnosed in the primary care setting. The device could also be used in the mental health care setting.

Indications for Use: The Medibio Depression Diagnostic Algorithm uses heart rate and actigraphy data obtained from third-party recording devices to aid in the diagnosis of major

depressive disorder. The device should only be used by a clinician and should be accompanied by a medical evaluation for a final diagnostic determination. The Medibio Depression Diagnostic Algorithm is not to be used as a stand-alone diagnostic device.

4-The study was completed in May 2018. Why did it take so long for the results?
Archie: The study was fully enrolled in April 2018 with last follow up in May 2018. We needed to perform study site close-out procedures, obtain the data, clean the data, build the master file and process the data. And that takes time.

5-Was the 60% benchmark figure set from the FDA discussion?
Archie: No, this is a threshold that Medibio calculated as the primary endpoint.

6-Why does the company think the FDA will look favorably when the hypothesis test was 60%?
Archie**:** The accuracy, sensitivity and specificity of 70%, 71% and 70% reported in our press release are considered superior to current physicians inter-rater reliability reference standard that ranges between 48%-64% for clinical specialist, and 30%-50% for general practitioners. Important to mention that DX04 Hypothesis Test wasn't selected and calculated based on reference standard but assigned by calculation during the initial study design. Using a physician inter-rater reliability reference standard of 55%, then our true hypothesis tested 58%. It is the inexact calculated selection of a hypothesis test that led to “failure” of the null hypothesis.

7-How will the study results play out for practicing clinicians?
Marie: We currently do not have any objective data available in clinical practice to support our diagnosis of psychiatric conditions. Our current method of diagnosis is currently based entirely on subjective data. Many factors interfere with diagnostic accuracy of mental health conditions based solely on subjective data, so a clinical support monitor with 70% accuracy will be very appreciated by clinicians who see psychiatric patients.
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This objective data will not only improve our diagnostic accuracy, but the objective data that was used to assist in diagnosis can then serve as the baseline for the ongoing monitoring of the patient’s response to treatment. A great advantage of ongoing use of this monitor, is that it allows for real-time assessment of a patient’s condition. Clinicians can access the data remotely so the early physiologic indicators of psychiatric decompensation can be found in real time and adjustments to their psychiatric treatment can take place early enough to prevent further decompensation. This approach will likely prevent many patients from experiencing psychiatric crises.

Currently patients must wait until their next scheduled psychiatric appointment in order to be assessed for appropriate medication changes or other treatment recommendations. By having to wait until an appointment, patients may have already experienced significant decompensation by the time they have their appointment. Treatment at that time becomes more reactive. Ongoing monitoring of patients with chronic depression allows for medication changes to be made that are more proactive rather than reactive.

8-We understand you were trying to get 200 participants in the study. Please explain why there was a high dropout rate?

Archie: Of notice, the FDA does not tell you what a given study sample size should be, we need to be clear on this point. The FDA **provides guidance** on things such as study design and regulatory compliance.

For this confirmatory study the inclusion and exclusion criteria were tighter, we have a number of initial screen failures, early study exit and lost to follow-up, these reduced the number of participants significantly. For example, subjects on certain medications (like benzodiazepine and antiarrhythmics, or those who had co-occurring medical conditions (like sleep apnea and sleep disturbances) were excluded from the study.

9-Can the company explain the rationale for the one sided test?
Melissa: Yes. A two-sided test is appropriate when you need to demonstrate that the new device is significantly higher or significantly lower than some performance level. We only needed to demonstrate to FDA that the sensitivity and specificity were significantly higher than 60%. That's a one-sided test. In general, one-sided tests require smaller sample sizes than 2-sided tests, so when FDA will allow their use, that's good.

10-Tell us about the statistical analysis plan used for analyzing the results?
Melissa: The main analysis plan was to test the hypothesis that the sensitivity was at least 60% and the specificity was at least 60%. The way the statistical test works is that the null hypothesis is that the sensitivity (specificity) is less than 60%, and you have to reject the null to show that the sensitivity (specificity) is 60% or better. Although the point estimates were higher than 60%, the sample sizes were too small (only about 40 in each group with 4 scans) to provide enough precision in the estimates to eliminate values lower than 60%. So the null hypotheses were NOT rejected. If we'd had larger samples, it's very likely that we'd have rejected the null hypotheses.

11-Would more sites in the trial impact the accuracy from previous estimates?
Archie: The accuracy of the DX04 is 70%. Increased number of sites will not impact accuracy, only the quality of the data obtained from each subject.

12-Why did you use a hypothesis test of .6 rather than something lower like previous studies?
Melissa: It was selected because FDA would not likely approve diagnostics that are not better than 50% by a clinically important amount. FDA would think that 55% was too close to a coin toss (a coin toss would be 50% accurate). **Was Medibio trying to reject the null hypothesis?** Yes**. Was it a one-sided test?** Yes. **What does this all mean to a normal person?** It means that we have some data indicating that the true sensitivity and specificity are better than 60%.

13-Why did you use a 95% confidence interval and not something lower? What were the Confidence intervals? How do the confidence intervals play into the results for FDA?
Melissa: A one-sided confidence interval using 95% has the same bound as a 90% two-sided confidence interval. We used 95% because that is what FDA requires. **What were the Confidence intervals?** The sensitivity confidence interval was .56 - .84 and the specificity was .57 -.85. **How do the confidence intervals play into the results for FDA?** The relationship between the confidence interval and the statistical test is that at a p-value of 0.05, the 95% confidence interval just touches the value you're testing. So if the p-value of

the test of 60% was 0.05, the lower bound of the confidence interval would be 60%. Because the p-value was LARGER than 0.05, it means that the lower bound of the confidence interval was LOWER than 60%.

14-Please explain why the p values were not statistically significant?
Melissa: The p values are related to the hypothesis test. The hypothesis test was not statistically significant probably because the sample size was a little too small to provide the precision we needed. If we had more patients it would have been statistically significant. We provided the data table to be transparent.

15-The DX03 study results reported in August 2017 showed accuracy of 82%. CI's were not presented. In hindsight was that a mistake?
Archie: Yes, in hindsight that could have been provided for clarification. DX03 was a performance feasibility study with sole purpose to estimate if the algorithm would perform moving forward. 61 subjects were enrolled, with 33 subjects in the final cohort and an average 1.7 scan per subject. The DX04 final cohort of 168 subjects averaged 3.3 scans.

16-Why the discrepancy between the latest results and the Ottawa results of November 2016?
Archie: This is comparing apples to oranges. The Ottawa data included a different subset of patients and data gathered which included sleep data, EKG, and polysomnography. The more objective data points obtained will result in high accuracy. The DXO4 study was a real world non-lab clinical study.

17-Four tests are required over a 2 week period to increase the effectiveness from 63% to 70%. Is this commercially viable (I.e. will GP's and other clinicians use the test if they are required to monitor a patient 4 times over a few weeks with approximately 70% sensitivity and specificity)?
Frank: Long-term monitoring of patients is very important as it gives us an extended period of data sets that, in turn, will provide more accurate results. Especially if retrogression in disease state.

18-Why did you include the table without explanations?
Archie: Previous releases did not include this level of data. We wanted to be transparent. We certainly learned a lesson here relevant to our communications. We provided data and tables to be more transparent, but now understand we should have included educational comments.

19-Can the business elaborate further around the context of the FDA submission and how this data is supportive?
Amy: We are unable to predict the FDA's response to our submission. We continue to work with them through the process, as they review the entire DeNovo application.

20. How does Medibio's algorithm compete with depression scales widely used in primary care settings such as the phq-9?
Frank: The phq-9 is designed to be disease driven, subjective evaluation at a point of time. Our objective data not only supports the diagnostic baseline it also analyzes changes that took place months before.

21-Can the business talk about how these results compare to other diagnostic tests that are being used?
Frank: As a DeNovo submission, there is no gold standard, and there are no predicate devices for us to compare. Medibio is building something unique in the industry.

22-Are there any other examples of DeNovo applications that were approved with 70% results?
Amy: Please note that each DeNovo application is typically tailored per the specific discussions the company has had with the FDA. There is not a one-size-fits-all approach with DeNovo applications. Some DeNovo applications have been granted approval even where the company's clinical trial did not meet its primary effectiveness endpoint. FDA has a case-by-case approach when it comes to DeNovo applications.

23-If the study is only 70% accurate, what happens to the 30% that are misdiagnosed?
Marie: Assuming this test is only being given to individuals who present to your clinic or ER with psychiatric symptoms the 30% without confirmation from the test would still be given some treatment recommendations, but their recommendations will likely be more general such as a recommendation for therapy. Therapy will provide additional collection of information from the patient that would likely eventually reveal the underlying condition and diagnosis, but just not as quickly as was obtained for the others through the monitor.

24-What do these results mean to a practicing psychiatrist? Will you use the 70% accuracy from the App instead of clinical judgement at 60%?
Marie: Having objective data with this high level of accuracy is a significant enhancement to support diagnosis which was never available previously and will definitely be used to enhance the diagnostic decision for a patient. This device will be especially useful for non-psychiatrists who struggle even more with making psychiatric diagnoses, but are increasingly being put in the position of needing to make psychiatric diagnosis and start psychiatric treatment.

CLOSING:

Peter: That is the end of the questions. I will turn the call over to Brian for a closing comment.

Brian: We again want to thank you all for taking time out of your schedules to join us on this teleconference. We understand and appreciate your attention to these study results and genuinely hope this session was educational for you. We will post the transcript on our website in the Company News section. Have a great day.