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World Sleep 2025: Alixorexton (ALKS 2680) Narcolepsy Type 1 Phase 2 Data

Sandra Coombs:

Welcome to the Alkermes plc conference call to discuss the results of the Vibrance-1 phase 2 study of alixorexton, in patients with narcolepsy type 1. With me today are Richard Pops, our CEO, Dr. Craig Hopkinson, our Chief Medical Officer, Dr. Marcus Yountz, Vice President of Clinical Development and special guest, Prof. Giuseppe Plazzi, the lead investigator for Vibrance-1.

A press release along with the slide presentation that we'll discuss today, are available on the Investors section of alkermes.com.

Our discussions during this conference call will include forward-looking statements. Actual results could differ materially from these forward-looking statements. Please see slide 2 of the accompanying presentation, our press release issued this morning, and our most recent annual and quarterly reports filed with the SEC, for important risk factors that could cause our actual results to differ materially from those expressed or implied in the forward-looking statements. We undertake no obligation to update or revise the information provided on this call or in the accompanying presentation as a result of new information or future results or developments. Our prepared remarks today will include data from our Vibrance-1 phase 2 clinical trial for alixorexton, formerly

known as ALKS 2680. These data may not be indicative of future data from this trial or results of other ongoing or future clinical trials.

After our prepared remarks, we will open the call for Q&A, and now I will turn the call over to Richard for some opening remarks.

Richard Pops:

We are glad to be joining you from the World Sleep Congress in Singapore where earlier today we shared data in three oral presentations from the phase 2 Vibrance-1 study of alixorexton in patients with narcolepsy type 1, or NT1. This study provides an important new increment of data, some of it entirely new information, not only for alixorexton, but for the broader field of orexin 2 receptor agonists for the treatment of narcolepsy.

I think we can say two things now with a new level of confidence. First, from a patient perspective, alixorexton has demonstrated compelling therapeutic benefits in patients with NT1, with a profound effect on excessive daytime sleepiness and significant improvements in fatigue and cognitive function, key drivers of patient quality of life and daily functioning. Taken together, we believe alixorexton has the potential to transform the treatment of NT1.

The second observation relates to competitive positioning. We see now that in a large, randomized, double-blind, multi-week study, alixorexton, administered once daily across

a range of doses, has demonstrated new, potential best-in-class features which may redefine what a leading agent in this category should deliver.

With data from a rigorous phase 2 study now in hand, we are confident in the profile of alixorexton in NT1 and are moving rapidly to initiate the phase 3 registrational program.

The key objective of the overall phase 2 program is to more fully elaborate the dose response curve of alixorexton across multiple safety, tolerability and efficacy measures – broadening the understanding of the therapeutic benefit of targeting this pathway and informing dose selection for phase 3. Vibrance-1 delivered on these goals and has revealed differentiating properties of alixorexton.

Today, Dr. Craig Hopkinson and Dr. Marcus Yountz will review detailed data from Vibrance-1. Craig is our Chief Medical Officer and he'll review the study design and primary and key secondary endpoints. Marcus is a neurologist, and Vice President of Clinical Development here at Alkermes and the clinical lead for the alixorexton program. He will provide an overview of the exploratory patient-reported outcome measures and a detailed discussion of the safety and tolerability profile. We are also delighted to be joined by Prof. Giuseppe Plazzi, the lead investigator for the Vibrance-1 study, to share his perspectives on the data and his experience with alixorexton in his patients.

Craig Hopkinson:

Today we will review a comprehensive dataset from the Vibrance-1 study in terms of both efficacy and safety. The study had a clear positive outcome. The results demonstrated alixorexton's significant effect on wakefulness and other important measures and a generally well tolerated profile.

One of the differentiating features of the Vibrance program is our intention to explore and broaden the definition of efficacy in patients with narcolepsy. This figure shows some of the many assessments included in Vibrance-1 to evaluate how alixorexton may address the clinical needs of patients with NT1.

In the study, we assessed the standard narcolepsy endpoints including the Maintenance of Wakefulness Test, Epworth Sleepiness Scale and weekly cataplexy rates along with safety and tolerability. We also collected additional data from a series of measures to further characterize the multiple dimensions of patients' response to treatment with alixorexton. Today, important data were presented relating to a broad range of symptoms that patients experience, including fatigue and cognition, as well as disease severity as assessed by patients themselves and by their clinicians.

As the field begins to recognize the broader potential of targeting the orexin pathway, these patient and clinician-reported outcomes take on new importance. We believe the ultimate value of alixorexton will be driven by its potential to deliver symptomatic relief across a more comprehensive spectrum of disease symptoms and to redefine the

expectations of what an effective medicine should achieve. Excessive daytime sleepiness is a central feature of narcolepsy and often the symptom most commonly associated with it. But NT1 patients often endure a broad set of debilitating symptoms including cognitive impairment and persistent fatigue. This is what makes the disease so devastating, and what makes the complete dataset from Vibrance-1 so compelling.

The Vibrance-1 phase 2 study was designed to provide a substantial dataset evaluating a range of doses of alixorexton in a multi-week study with well-powered cohorts of patients with NT1.

This six-week, double-blind, placebo-controlled, parallel design study evaluated three doses of alixorexton vs. placebo, followed by an open-label extension. We enrolled a total of 92 patients across 45 sites in the U.S., Europe and Australia. After washing out of their current narcolepsy medications for two weeks, patients were randomized to one of three once-daily dose levels of alixorexton: 4, 6, or 8 mg, or placebo.

The primary endpoint of Vibrance-1 is the change in mean sleep latency on the Maintenance of Wakefulness Test, or MWT, compared to placebo at the end of the six-week, randomized, double-blind period. Key secondary endpoints included the Epworth Sleepiness Scale and weekly cataplexy rates.

Following the double-blind period, patients had the opportunity to enter a seven-week open-label extension which included the option to adjust their dose. This feature provided valuable information regarding patient preference and informs our dose

selection for phase 3. Those who completed the open-label period had the option to enroll in a separate long-term extension study, for up to two years, which is currently ongoing.

In terms of baseline characteristics, these NT1 patients were highly symptomatic. The mean sleep latency on MWT at baseline was approximately 3 minutes, and the mean Epworth score was 18.5, reflecting severe excessive daytime sleepiness. With respect to cataplexy, on average, the study population reported 26 cataplectic events per week at baseline. As you can see, high variability was observed in patient reported weekly cataplexy rates, which we will discuss further when we review the data. And, on the Narcolepsy Severity Scale, patients reported a mean total score of 31.3 at baseline, which corresponds to severe narcolepsy symptoms.

We had a strong completion rate with 99% of subjects randomized completing the six-week double-blind period.

Turning now to the efficacy results, starting with the primary endpoint. The MWT is a standardized, quantitative measure of how long a patient can stay awake during a 40-minute test period in an environment that is conducive to sleep. The tests are conducted at 2, 4, 6 and 8 hours post-dose and the mean score is calculated by averaging the results of the four tests. While the MWT is less frequently used in the real-world clinical setting, it is an important objective endpoint commonly used for regulatory purposes.

The table on the right shows the pre-specified analysis. At week six, alixorexton showed statistically significant and clinically meaningful improvement from baseline in mean sleep latency compared to placebo at all doses tested.

The graph on the left shows observed mean sleep latency, at baseline and at week six, by treatment group. At baseline, participants fell asleep within approximately 3 minutes, consistent with the broader NT1 patient population. At week 6, the placebo group did not demonstrate any benefit, while for the alixorexton treatment groups, the data demonstrated a dose-dependent improvement in wakefulness. On an observed basis, the 4, 6, and 8 mg dose groups were associated with mean sleep latency of approximately 24, 26 and 28 minutes, respectively, well above the 20-minute threshold considered normative wakefulness.

These data represent mean values across each alixorexton dose cohorts. However, individual patients have differing responses so it is instructive to look deeper, beyond the average values. At week 6, a significant majority -- approximately 75–80% of subjects – achieved normative wakefulness. Some patients across each alixorexton dose group, achieved the maximum 40 minutes on the MWT across the full eight-hour assessment period. And, in the 8 mg group, the majority of subjects achieved an observed mean sleep latency of 30 minutes or greater. These findings underscore a central principle: patients differ in their physiological response. This is the logic underpinning our strategy to develop multiple effective doses.

Turning to the key secondary endpoints. First, the Epworth Sleepiness Scale, or ESS. ESS is a patient-reported symptom questionnaire. Unlike the MWT, this scale is widely used in the clinic as a diagnostic tool to assess excessive daytime sleepiness. ESS is useful in that the seven-day look back period provides a holistic view of patients' sleepiness beyond the eight-hour MWT test period. Higher scores indicate a greater likelihood of falling asleep with a score of 10 or below considered normal.

The graph at the left shows the mean scores for each study arm over the 6-week double-blind period. At baseline, patients in Vibrance-1 reported mean ESS scores of approximately 18.5, reflecting excessive daytime sleepiness. Reductions in ESS were observed with alixorexton across all doses starting as early as week 2, the first timepoint measured. The mean ESS scores remained below 10, indicating normalization of daytime sleepiness during the six-week treatment period.

The table on the right reflects the pre-specified analysis. All doses of alixorexton given once daily demonstrated statistically significant improvements from baseline in excessive daytime sleepiness compared to placebo. The 6 mg and 8 mg doses showed the greatest reductions in sleepiness, with improvements of 11 to 12 points compared to baseline, while placebo improved by 3 points during that window.

At the time of the analysis of the topline results of the double-blind period, 59 patients had completed the entire 13-week study including the seven-week open-label

extension. ESS was collected at weeks 8 and 13, as shown on the shaded area on the right-hand side of this graph. Recall that in the open-label extension all patients started on 6 mg of alixorexton and could make dose adjustments between weeks 6 and 8. The dotted lines correspond with the dose that patients had received in the double-blind treatment period. Two key observations: First, the improvements with alixorexton in mean ESS scores reported during the initial six-week period were sustained through week 13. Second, patients who transitioned from placebo to active treatment in the open-label extension demonstrated improvements in ESS comparable to those randomized to alixorexton in the double-blind period, highlighting the drug's consistent profile. We will present the full data set from the open-label extension at a future medical meeting.

Now let's look at cataplexy. In addition to excessive daytime sleepiness, NT1 patients can experience a sudden involuntary loss of muscle tone called cataplexy. Vibrance-1 evaluated mean weekly cataplexy rates as a key secondary endpoint. Baseline cataplexy rates varied widely across individuals, with some subjects reporting several hundred episodes per week.

The graph on the left shows median weekly cataplexy rates at baseline and week 6. Median cataplexy rates numerically decreased from baseline across all groups, including placebo, with the alixorexton-treatment groups reporting median rates as low as one cataplexy event per week in the 6 mg arm.

The table on the right shows the pre-specified analysis: the incidence rate ratios for each group at week 6 compared to placebo. Here alixorexton demonstrated numerical and clinically meaningful improvements across all doses tested and, on the pre-specified analysis, the 6 mg dose met the threshold for statistical significance and demonstrated a nearly 70% reduction in event rate compared to placebo.

Given the numerical changes on the left, it may be surprising that statistical significance was achieved only at one dose. This was primarily driven by significant variability in this patient-reported outcome and a small number of outliers.

Another way to interpret the cataplexy data is by examining the proportion of patients who experienced no cataplectic events during the assessment period. On this analysis, 24% of patients in the 4 mg group and more than 40% of patients in both the 6 and 8 mg groups achieved 100% reduction in cataplexy events during week 6 of the study. This compared to only 5% of patients in the placebo arm.

We are confident in alixorexton's effect on controlling cataplexy. Collectively, these data show a clinically meaningful improvement on cataplexy across all doses tested. We learned a great deal in phase 2 related to the implementation of this assay and we will apply these key learnings in our phase 3 program.

Having reviewed the primary and key secondary endpoints related to efficacy. I'll now hand the call over to Marcus for a review of the exploratory patient-reported outcome

measures across disease severity, fatigue and cognition, as well as a review of the safety and tolerability profile.

Marcus Yountz:

While excessive daytime sleepiness is the hallmark symptom of narcolepsy, many patients also experience other symptoms, such as fatigue and cognitive dysfunction. These can result in significant morbidity as well as impaired quality of life.

The disease of NT1 is caused by a deficiency of orexin. What is so exciting about alixorexton is its potential to address the underlying cause of the disease by effectively replacing the deficient neuropeptide to deliver a broad spectrum of potential therapeutic benefits. These effects derive not only from increased wakefulness, but from downstream engagement of brain circuitry related to mood, fatigue and cognition. The assessments I'll discuss today were exploratory and as such, p-values reflected in the slides are nominal.

So, let's start with measures of overall disease severity, from the patients' own perspective.

The Narcolepsy Severity Scale, or NSS, is a validated instrument that was specifically developed to assess the frequency and impact on daily life over the past seven days of five key narcolepsy symptoms -- excessive daytime sleepiness, cataplexy, nighttime

sleep disturbance, hallucinations, and sleep paralysis -- to determine disease severity ranging from “Mild” to “Very Severe”.

At baseline, patients enrolled in the Vibrance-1 study were highly symptomatic, reporting average NSS scores of approximately 31 points across the study population, which corresponds to “Severe” disease.

Looking at the chart on the left, at week 6, patients in the 6 and 8 mg dose groups achieved average scores in the “Mild” disease range—the lowest severity category of the NSS, indicating clinically meaningful reductions in narcolepsy symptom severity. In the table at the right, we see that the improvements from baseline at week 6 were statistically significant compared with placebo for all doses of alixorexton.

Let’s take a closer look at the reported shifts in severity over the 6 weeks.

On the left you see each treatment group at baseline, at which point many patients reported “Moderate” or “Severe” disease as you can see in light blue and yellow. Moving to the right, at Week 6, most patients across all doses of alixorexton reported “Mild” disease severity, indicated by dark blue. You will see similar representations for the other patient-reported outcomes, so keep in mind that on these charts bluer always means better.

The study also provided entirely new and exciting findings related to fatigue and cognition. These are among the most debilitating symptoms patients with narcolepsy experience, and they are distinct from excessive daytime sleepiness.

Let's look at findings related to fatigue. Fatigue is reported by the majority of patients with narcolepsy. While fatigue and sleepiness may be related, patients distinguish between them – with fatigue often being described as a feeling of mental and physical exhaustion that is not improved with sleep alone.

PROMIS-Fatigue is a comprehensive instrument that has been broadly used across several disease states. Scores less than 55 signify normal levels of fatigue, while higher scores signify progressively more severe fatigue. This graph shows the PROMIS-Fatigue scores at each time point measured. At baseline, patients enrolled in Vibrance-1 had scores consistent with "moderate" fatigue. At the first time point measured, mean scores for all alixorexton dose groups fell below 55 into the normal range, and these were sustained through week 6. The improvements in fatigue scores were statistically significant compared to placebo for all alixorexton dose groups.

Now let's turn to cognition. In speaking with narcolepsy patients, brain fog and cognitive complaints are among the most commonly mentioned challenges they face. In the study, we used an established patient-reported measure, the British Columbia Cognitive Complaints Inventory, or BC-CCI, to assess patients' perception of the severity of their cognitive impairment. The BC-CCI is multi-dimensional and evaluates several areas of

cognition that may be impaired, such as memory, attention, and word finding, among others. Scores range from 0 to 18, with higher numbers representing greater severity, and with scores below 4 indicating minimal or no cognitive complaints.

Alixorexton significantly reduced the severity of cognitive impairment across all doses tested.

Mean cognitive impairment scores fell within the “none or minimal” impairment category across all timepoints and at all doses—effectively achieving normalization for most patients. Improvements were observed at the first time point measured and sustained through week 6. In addition to being clinically meaningful, the improvements from baseline at week 6 were highly statistically significant compared to placebo.

Another way of looking at this data is by the proportion of patients falling into the different severity categories of the BC-CCI. On this slide, baseline is shown on the left. Again here, blue colors represent more mild symptoms. At week 6, shown on the right, most patients treated with alixorexton, across all doses, reported “none or minimal” cognitive impairment.

We also looked at the expanded version of the BC-CCI which includes additional questions related to the perceived impact of cognitive impairment on work, relationships and daily activities. Similar to the severity items, improvements were observed at the

first timepoint measured and were sustained through the six-week period. At week 6, the improvements were statistically significant for all alixorexton doses tested.

Taken together, these results suggest that patients who received alixorexton experienced statistically significant and clinically meaningful improvements in cognitive functioning.

Vibrance-1 also included a collection of clinician and patient global impression assessments, commonly referred to as CGI and PGI. Data from these assessments were similarly striking and were presented as part of today's oral presentations. These presentations are available on our website for reference.

From a clinical perspective, the results of these patient-reported outcomes are compelling due to the robustness and, particularly, the consistency of effect and durability – across all doses of alixorexton as well as across the various assays that were used in the study. This is the first time that we've seen data from the orexin class on these fatigue and cognition scales. We believe this differentiates alixorexton from other development programs and builds upon the evidence base that orexin 2 receptor agonists with appropriate pharmaceutical properties could have broad potential utility across a range of neurological or neuropsychiatric disorders where the orexin system may be implicated.

Turning to safety and tolerability. Vibrance-1 was our first opportunity to assess safety and tolerability over multiple weeks of repeat dosing in a randomized, double-blind study as well as to start building the long-term safety database for alixorexton. In the study, alixorexton was generally well tolerated at all doses tested. As Craig mentioned, study retention was strong with 99% of patients completing the double-blind period. One patient randomized to the 8 mg dose discontinued after reporting treatment-emergent adverse events, or TEAEs, within the first few days of treatment. No treatment emergent serious adverse events were reported. Most TEAEs were mild to moderate in severity. The most commonly reported TEAEs - pollakiuria (or urinary frequency), insomnia, salivary hypersecretion, micturition urgency (or urinary urgency), and blurred vision - were consistent with on-target effects of orexin 2 receptor agonists and were largely associated with treatment initiation and resolved without medical intervention.

Understanding the temporal nature of these events is an important element of the profile, so let’s take a closer look at the onset and duration of some of these. First, let’s discuss urinary events, including frequency and urgency. These events were primarily mild and generally more persistent during the six-week double-blind period. Importantly, none led to discontinuation of study drug.

Next is insomnia. The vast majority of insomnia events occurred and resolved within the first week of treatment. This was consistent with our expectation and what has been observed in other multi-week studies of orexin 2 receptor agonists.

Events of blurred vision were dose-dependent and occurred primarily at the 8 mg dose, with infrequent events at the 4 and 6 mg doses as well as in placebo-treated patients. Events were mostly mild and intermittent and largely occurred and resolved within the first three days of treatment. This also held true for the events that were reported beyond week 1, mostly mild and intermittent in nature. In other words, not necessarily occurring on a daily basis and episodic as opposed to continuous.

As previously disclosed, all patients were subject to thorough ophthalmic assessments at baseline and at the end of the double-blind period. No clinically meaningful treatment-emergent changes were observed on these exams in the alixorexton treatment groups. Further, and importantly, no clinically meaningful changes in patients treated with alixorexton were reported across hepatic or renal parameters, vital signs or ECGs.

Overall, these safety and tolerability data are encouraging and add to the growing body of evidence supporting the use of orexin 2 receptor agonists in the treatment of NT1. Taken together with the strong efficacy demonstrated in Vibrance-1, the emerging benefit-risk profile for alixorexton is clear and compelling.

Craig Hopkinson:

As a testament to the generally well tolerated profile and robust efficacy observed in the six-week, double-blind period, more than 95% of study subjects chose to roll into the open-label extension. We will present a full analysis of the open-label extension period at a future medical conference but today we will share a few initial observations.

First, the design of the open-label extension and the data it yields about patient preference are some of the most interesting and important findings from the study. After completing the six-week double-blind period, all subjects started the open-label extension at the 6 mg dose and then, in consultation with investigators, had the option to remain at 6 mg, move down to 4 mg or move up to 8 mg.

The results provide us with new insights into patient dose preference and the safety and tolerability profile.

Let’s start with the dose adjustment trends.

Starting with the placebo cohort. Upon initiating active treatment in the open-label extension at the 6 mg dose, the majority of these subjects elected to remain at that dose throughout the open-label period. Now let’s look at those patients treated with alixorexton in the double-blind period. Of subjects that had been randomized to the 4 mg dose, approximately two-thirds chose to move up to 8 mg during the flexible dosing period. Of subjects that had been randomized to 6 mg, approximately two-thirds chose to remain at that dose in the open-label extension, and approximately one-third escalated to 8 mg. Of the subjects that had been randomized to 8 mg, after stepping down to 6 mg at the start of the open-label extension, approximately two-thirds chose to return to the 8 mg dose, and about one-third elected to remain at the 6 mg dose.

Overall, five subjects of 90 elected to move down to the 4 mg dose in the open-label extension. The remaining 85 subjects chose the 6 and 8 mg doses at approximately equal rates. This result reinforces the hypothesis that patients will have varying preferences and underscores the importance of providing a range of doses to accommodate individual patient needs.

Turning to the initial safety and tolerability findings from the open-label extension. Overall, the incidence of TEAEs was lower in the open-label extension than in the double-blind treatment period.

Consistent with the findings from the six-week double-blind period, alixorexton continued to be generally well-tolerated. Treatment-emergent adverse events were mostly mild to moderate and no serious treatment-emergent adverse events were reported.

Among the TEAEs that were most commonly reported in the double-blind period that Marcus discussed, in the open-label extension, onset of new events was primarily associated with treatment initiation – in other words, events occurred primarily in patients that had been randomized to placebo in the double-blind period who started alixorexton at the 6 mg dose for the first time in the extension.

In the open-label extension, we also learned that for patients with prior exposure to alixorexton, new onset of these TEAEs was low.

For example, looking at the 46 patients that elected to move up to the 8 mg dose in the extension -- while on the 8 mg dose, new onset of the TEAEs most commonly reported in the double-blind period was minimal, with no new events of pollakiuria, insomnia, salivary hypersecretion or blurred vision reported.

These data build upon the findings from the double-blind period and demonstrate a strong safety and tolerability profile. They are invaluable as we finalize our phase 3 dose strategy.

On behalf of Alkermes, I'd like to thank all the investigators and patients, along with their families, for participating in this groundbreaking study. These data represent a substantial new contribution to narcolepsy research.

And now I'd like to welcome Prof. Giuseppe Plazzi, the lead investigator in the Vibrance-1 study. Dr. Plazzi, thank you for being here to share your clinical insights on the clinical relevance of the Vibrance-1 data.

Prof. Giuseppe Plazzi:

The data presented at World Sleep today represent a significant milestone in the treatment of narcolepsy. The orexin 2 receptor agonist class has the potential to transform how patients with NT1 are treated and the alixorexton data presented today reinforce and further define this potential.

The detailed Vibrance-1 dataset highlights the robust efficacy of once-daily alixorexton in improving wakefulness and reducing excessive daytime sleepiness in patients with narcolepsy type 1, along with a generally well tolerated safety profile. What you begin to see in this dataset are additional, nuanced aspects of the NT1 patient experience. Narcolepsy is a debilitating disease that goes far beyond the cardinal symptoms of excessive daytime sleepiness and cataplexy. Patients often take multiple medications and suffer from debilitating cognitive dysfunction and fatigue, which interferes with their daily activities.

In Vibrance-1, untreated at baseline, patients were highly symptomatic and reported severe disease. The rapid and profound effects that alixorexton demonstrated in this study are truly exciting. With this class of medicines, I often say that patients are awakened, but this encompasses much more than just wakefulness. As a physician, it is particularly satisfying to see how patients are transformed with effective treatment.

I'll offer a few clinical perspectives on the data reported today and then will be happy to take questions during the Q&A.

In terms of wakefulness, it is encouraging to see the magnitude and consistency of effect across MWT and Epworth. First on MWT, I'm very pleased with the results. Alixorexton treatment groups achieved normative wakefulness on the MWT, and as a clinician, this is the goal. While MWT is a helpful assay in the clinical trial setting,

maximizing MWT is not a key objective when treating patients, and pushing too high may result in adverse events. We should look at MWT in the context of other end points.

Epworth and NSS scores provide important additional dimensions to the patient experience, and as the data presented today demonstrated, patients treated with alixorexton achieved normal wakefulness on ESS and symptoms in the lowest severity category on the NSS. These reinforce the MWT data.

In terms of cataplexy -- this is an important clinical symptom but it is nuanced and even many physicians may not recognize it. The clinical assay itself is subjective and variable in that the way patients identify and count events can vary. For example, reporting multiple separate events that are actually part of the same cataplectic episode. When I look at the overall data from the Vibrance-1 study and from my own experience, alixorexton had a clear effect on cataplexy. I think this can be more clearly elaborated in phase 3.

In patients with NT1, when the orexin circuity is reactivated you can see a number of effects –wakefulness and cataplexy are only two elements. NT1 patients often experience fatigue and cognitive dysfunction that can impair their daily functioning. From a clinical perspective, the cognition and fatigue data captured in Vibrance-1 are compelling and begin to provide a more complete picture of alixorexton's potential therapeutic benefit to patients. Patients often forgo many opportunities for education

and professional development due to their symptoms and this could have a real impact for patients and the opportunities this may enable them to pursue.

The complete safety and tolerability profile observed in Vibrance-1 is encouraging and was consistent with what I observed with my patients in the study. With adverse events that were mostly mild to moderate, and largely associated with treatment initiation, this is a very manageable profile.

I'm pleased with the outcome of the study. These data underscore alixorexton's potential to be an important new treatment option for NT1 and to reduce the broader disease burden of this complex neurological disorder.

Richard Pops:

It's been an exciting day here at World Sleep in Singapore. We've had the privilege of presenting our phase 2 data for alixorexton in NT1 and engaging directly with leading sleep medicine experts. Now, based on our Vibrance-1 data and a clear understanding of the competitive landscape, we believe alixorexton has a differentiated and potential best-in-class profile that could redefine the standard of care in narcolepsy type 1. But NT1 is just the beginning.

In narcolepsy type 2, where we expect to be first-in-class, our phase 2 Vibrance-2 study will generate the largest dataset to date for an orexin 2 receptor agonist in NT2. We recently completed enrollment in that study and plan to have topline data later in the fall.

Data from Vibrance-3, our phase 2 study in idiopathic hypersomnia, will follow next year.

In parallel to these phase 2 studies, preparations for phase 3 are underway and we are working to initiate the phase 3 program in narcolepsy as quickly as possible. Alkermes is well positioned as a leader in development in this exciting new therapeutic category in sleep disorders and beyond.

With that I will turn the call back to Sandy to manage the Q&A.
