*October 25, 2023*

**Alkermes Q3 2023 Earnings Conference Call Prepared Remarks**

**Sandy Coombs:**

Welcome to the Alkermes plc conference call to discuss our financial results and business update for the quarter ended September 30, 2023 as well as initial clinical data related to ALKS 2680 that we presented during this week's World Sleep Meeting. With me today are Richard Pops, our CEO, Iain Brown, our CFO, Todd Nichols, our Chief Commercial Officer and Dr. Craig Hopkinson, our Chief Medical Officer. During today's call, we will be referencing slides which are available on the investor events section of our website.

Before we begin, I encourage everyone to go to the Investors section of alkermes.com to find our press release, related financial tables and reconciliations of the GAAP to non-GAAP financial measures that we'll discuss today. We believe the non-GAAP financial results, in conjunction with the GAAP results, are useful in understanding the ongoing economics of our business.

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 initial patient data from our phase 1 clinical trial for ALKS 2680. These data may not be indicative of future data from this trial or results of future clinical trials.

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

**Iain Brown:**

Thank you, Sandy, and hello everyone.

I am pleased to report solid results for the third quarter that demonstrate the financial strength of the business. The quarter was highlighted by year-on-year growth across our proprietary commercial products, solid contributions from manufacturing and royalty revenue streams, disciplined expense management and strong GAAP and non-GAAP profitability. With the favorable outcome of the Janssen arbitration earlier this year, the successful settlement of the VIVITROL patent litigation and the expected completion of the separation of the oncology business in the coming weeks, the potential of the business to deliver enhanced profitability has come more clearly into focus. This has been our plan and it is gratifying to see it begin to take shape.

For the third quarter, we generated total revenues of $380.9 million, compared to $252.4 million in the same period in the prior year. This reflects the reinstatement of royalties on U.S. sales of

the long-acting INVEGA products and solid performance across our proprietary product portfolio, which grew 16% year-over-year.

Starting with VIVITROL, net sales in the quarter were $99.3 million, reflecting 3% growth year-over-year, driven by the alcohol dependence indication. Inventory in the channel was stable and gross-to-net deductions were consistent and within normal ranges for the quarter.

Moving on to the ARISTADA product family. For the quarter, ARISTADA net sales increased 8% year-over-year to $81.8 million, primarily driven by underlying demand. Inventory in the channel was stable and gross-to-net adjustments were unchanged sequentially.

LYBALVI net sales for the quarter were $50.7 million, up 8% sequentially. Underlying prescription growth was 10%, on a months of therapy basis. During the quarter, inventory in the channel decreased by approximately $1.3 million and gross-to-net adjustments of 25.1% reflected the continuation of our contracting strategy in the commercial space and a one-time favorable Medicaid adjustment.

Moving on to our manufacturing and royalty business. In the third quarter, we recorded manufacturing and royalty revenues of $149.1 million, compared to $52.9 million in the same period in the prior year. Revenues from the long-acting INVEGA products were $76.1 million compared to $26.7 million in the same period in the prior year, reflecting the favorable resolution of the arbitration related to these products earlier this year. Revenues from VUMERITY were $34.6 million, compared to $26.3 million in the same period in the prior year.

Turning to expenses, total operating expenses were $337.1 million for the third quarter, compared to $313.0 million in the same period in the prior year.

R&D expenses for the third quarter decreased to $97.1 million, compared to $100.4 million for the same period in the prior year. This reflects lower external spending across the nemvaleukin and LYBALVI clinical programs, partially offset by increased investment in the ALKS 2680 clinical program.

SG&A expenses increased to $169.4 million, from $152.8 million for the same period in the prior year, reflecting continued investment in the launch of LYBALVI, particularly the DTC campaign, and certain non-recurring expenses related to the separation of the oncology business.

I'm pleased to report that our topline results, combined with our continued focus on disciplined operating expense management, delivered GAAP net income of $47.8 million, and non-GAAP net income of $109.5 million for the quarter.

Today we are reiterating our financial expectations for 2023 that we provided in our press release on June 6, 2023. As a reminder, our financial expectations reflect the combined neuroscience and oncology business for the full year.

Turning to our balance sheet, we are in a strong financial position, as we ended the third quarter with approximately $996 million in cash and total investments, and total debt outstanding of approximately $291 million. We currently expect that, upon separation, Alkermes will provide

$275 million of cash to Mural Oncology, which we believe will enable Mural to fund its operations through topline data readouts for ARTISTRY-6 and ARTISTRY-7 and into the fourth quarter of 2025. In the coming weeks, we will provide additional information regarding the separation and distribution of Mural shares to our shareholders.

Post-separation, Alkermes will emerge as a pure-play neuroscience business with enhanced profitability and a strong balance sheet. Our focus will remain on the execution of our strategic priorities, and disciplined management of our cost structure, as we invest in those opportunities that we believe will drive future growth, including the ALKS 2680 development program and the continued launch of LYBALVI.

And with that, I'll hand the call over to Todd for a review of the proprietary commercial products.

**Todd Nichols:**

Thank you, Iain. Good morning, everyone.

I am pleased to share that we delivered solid year-over-year growth of 16% across our proprietary commercial portfolio in the third quarter. Our performance during the quarter reflects continued execution of our commercial strategy against the backdrop of some summer seasonality in the psychiatry and addiction treatment markets. We expect growth to accelerate in the fourth quarter and reiterated our expectations for our 2023 proprietary product revenues today.

Starting with LYBALVI. Net sales increased 8% sequentially to 50.7 million dollars. Prescriptions grew to approximately 42,000 TRxs for the third quarter, reflecting 10% sequential growth which was ahead of other entrants in the branded oral antipsychotic market. We expect that growth will accelerate as we head into the fourth quarter, driven by a strong focus on execution, our direct-to-consumer campaign and underlying seasonal trends, and we are encouraged by prescription trends over the past several weeks.

During the quarter, prescriber breadth continued to expand. In our recent market research, healthcare providers cited LYBALVI's efficacy, weight gain profile and patient outcomes as key drivers for their increased prescribing, which is encouraging feedback as we think about brand awareness and potential future prescribing patterns.

In terms of market access, in Medicare and Medicaid, there is a pathway to access for all patients. In the commercial channel, there were no changes to our commercial access profile during the quarter and we expect the access profile to remain unchanged for the remainder of 2023. We have ongoing discussions with the commercial payers and have designed our commercial access strategy to best support the long-term growth of the brand, balancing volume growth and the profitability of each unit.

As we advance our efforts to drive awareness, our direct-to-consumer campaign is ongoing with increased ad placement in the Fall months, in line with TV viewership trends. While it will take time to see the full impact, leading indicators on the effectiveness of the DTC are encouraging. Specifically, we are monitoring the impact of our DTC campaign on internet search metrics,

website visits, provider and patient awareness levels, and patient requests. We are excited by the opportunity for LYBALVI and are laying the foundation for long-term growth.

Turning to the ARISTADA product family, net sales in the third quarter grew 8% year-over-year to 81.8 million dollars, driven primarily by demand growth of approximately 8% on a months-of-therapy basis. We expect this market will continue to be dynamic and our team will continue to focus on highlighting ARISTADA's differentiated value proposition, including its once every two-month dosing option and the ARISTADA INITIO initiation regimen, both of which are supported by clinical data from our ALPINE study.

Turning to VIVITROL. Net sales in the third quarter increased approximately 3% year-over-year to 99.3 million dollars. The alcohol dependence indication was VIVITROL's primary growth driver and accounted for approximately two-thirds of the VIVITROL volume. Importantly, against the backdrop of growth in the alcohol dependence treatment market, prescriber breadth for VIVITROL has continued to expand in that indication, which has driven new patient starts over recent quarters.

As we think about the long-term opportunity for the brand, during the quarter, we were pleased to come to a settlement agreement with Teva to resolve our patent litigation related to VIVITROL. Under the terms of the agreement, Teva will be able to market a generic version in the U.S. beginning in January 2027, or earlier under certain customary circumstances. With this agreement, we are able to appropriately plan for the continued commercialization of VIVITROL

and believe that the product will continue to be an important element of our growth and profitability for the next several years.

Taking a step back, we are focused on executing our brand strategies for all three products and on delivering on our net sales expectations for 2023 across the portfolio.

Serious mental illness and addiction are complex conditions with unique and often challenging treatment paradigms that require well-resourced and dynamic commercial efforts to support patient access and drive growth. Our commercial infrastructure is a strategic asset – one that can be leveraged in additional opportunities in these disease spaces, as well as in other therapeutic categories, including those that may emerge from our development pipeline or future business development opportunities. With that, I'll pass the call to Craig to discuss our ALKS 2680 development program.

**Craig Hopkinson:**

Thank you, Todd.

I'm pleased to be joining you this morning from the World Sleep meeting where earlier this week, we presented the first clinical data for ALKS 2680, our novel, investigational orexin 2 receptor agonist for the treatment of narcolepsy.

The orexin pathway has been established to be closely linked to the pathology of narcolepsy. Orexins are neuropeptides that serve as important regulators of the sleep/wake cycle by promoting wakefulness and suppressing REM sleep. In particular, narcolepsy type 1, or N-T-1, is associated with an absence or significant deficiency in orexin concentrations and the presence of cataplexy. People living with narcolepsy who do not experience cataplexy have what is called narcolepsy type 2 or N-T-2.

ALKS 2680 was designed to be an orally bioavailable orexin 2 receptor agonist with potency 10 times greater than the natural orexin A peptide, and greater than 5000-fold selectivity relative to the orexin 1 receptor. The molecule was designed to address the underlying pathology of narcolepsy and to deliver durable and quality of daytime wakefulness and cataplexy control, an acceptable safety and tolerability profile, and a wide therapeutic range that can accommodate the different doses potentially needed for NT1 and NT2. The molecule was also designed to exhibit a pharmacokinetic and pharmacodynamic profile that mirrors the natural sleep/wake cycle, with a low therapeutic dose and once-daily oral dosing.

The clinical investigation of ALKS 2680 follows encouraging preclinical data. These preclinical data were also shared in an oral presentation this morning at the World Sleep meeting. Today, I will focus on a review of the phase 1 safety and tolerability data of ALKS 2680 in healthy volunteers and share initial safety and efficacy findings from patients with Narcolepsy Type 1.

It is gratifying that, in our clinical experience to date, ALKS 2680 has behaved as we would have expected based on our extensive preclinical work. We are pleased with the clinical profile that is emerging, both in terms of safety and tolerability as well as therapeutic activity observed in patients.

The study design is outlined on slide 15. The phase 1 study began with single and multiple ascending dose evaluations in 80 healthy volunteers to assess safety and tolerability as well as the pharmacokinetic and -dynamic profile of ALKS 2680. This study is double-blind and placebo-controlled. The single-ascending dose, or SAD, tested single doses of ALKS 2680 up to 50 mg. In the multiple-ascending dose, or MAD, subjects received 10 days of once-daily doses up to 25 mg.

Moving on to slide 16. From a safety and tolerability perspective, I'm pleased with the profile that we observed for ALKS 2680 in healthy volunteers. ALKS 2680 was generally well tolerated across all doses tested and there were no serious or severe adverse events. Most adverse events were mild, occurred early, were transient and resolved without medical intervention or treatment interruption.

In the SAD, the most common AEs deemed to be drug related were dizziness, pollakiuria, which means increased frequency and urge to urinate, nausea and visual disturbances, and most were observed at or above the 15mg dose. In the MAD, the most common AEs were insomnia, dizziness, pollakiuria and visual disturbances, and most were observed at or above the 8 mg

dose. The visual disturbances were described as blurred vision and increased light sensitivity. As I mentioned, these AEs were transient, resolved with continued dosing of ALKS 2680 in the multiple ascending dose study, and did not prevent continued dose escalation. There were no safety signals identified in vital signs, laboratory parameters or ECG. No hepatotoxicity signals were observed at any dose level.

We will continue to accumulate safety data over the course of the development program. This will include continuing dose escalation in the SAD and the MAD in order to fully characterize the safety and tolerability profile of ALKS 2680, as a maximum tolerated dose has not yet been identified.

In terms of the pharmacokinetic profile on slide 17, we achieved a key design objective supporting once-daily dosing of ALKS 2680 and a profile that mimics the natural sleep/wake cycle with a half-life of 8 to 10 hours. In the top panel you can see that systemic exposures increased proportionately with dose, however with a blunted cmax profile as depicted in the lower graph – both of these features were explicit design intentions. The metabolic profile was also consistent with our design objectives. In the study, two metabolites were observed. These metabolites were consistent with those observed in preclinical studies. Neither contributed to pharmacologic activity nor were they reactive.

Collectively, data from the SAD and MAD evaluations supported the dose levels selected to move forward into the phase 1b evaluations in patients. This part of the study is enrolling

patients with narcolepsy type 1, narcolepsy type 2 or idiopathic hypersomnia, with up to 8 patients per group. Earlier this week, we shared data from the first cohort of 4 narcolepsy type 1 patients – which was specified and powered to detect any significant effects and dose responses at this interim analysis.

Starting with the study design on slide 18, following a 2-week washout period of existing medications, patients were randomized to a cross-over design where each received placebo, 1, 3, and 8 mg of ALKS 2680 with a 1-day washout period in between each dosing day.

The primary endpoints are safety and tolerability. However, the phase 1b also offers the first opportunity to assess proof of concept efficacy of single doses of ALKS 2680, compared to placebo and baseline, within the same subjects, via the Maintenance of Wakefulness test. In terms of baseline characteristics outlined on slide 19, the patients studied demonstrated severe narcolepsy symptoms.

Next on slide 20, ALKS 2680 was generally well tolerated across all doses tested in the NT1 patients. All AEs were mild, only occurred at the 8 mg dose and were largely on target. Note that the most common AE was insomnia, which is directly related to the drug's activity. This is what we were looking for. The occurrence of insomnia at the 8 mg dose was useful in helping us to narrow the planned dose range for future clinical development in NT1. Pollakiuria and salivary hypersecretion occurred in two of the subjects. These AEs are expected on-target effects for the orexin pathway. There were no serious adverse events, nor any AEs leading to discontinuation.

Additionally, there were no clinically meaningful, treatment-emergent changes in laboratory parameters or ECG.

Turning to slide 21 and the first assessments of ALKS 2680 in the maintenance of wakefulness test. The 40-minute maintenance of wakefulness test, or MWT, is administered every two hours post-dosing. The mean score is calculated by averaging the results of the tests conducted at hours 2, 4, 6 and 8 post-dose. Prior to dosing, patients demonstrated a mean MWT baseline score of three minutes, meaning that they fell asleep within three minutes. At all doses tested, and in all patients, ALKS 2680 significantly improved mean sleep latency, or the time these patients were able to remain awake, compared to baseline. There was a clear dose response, with mean MWT improvements compared to baseline of 18, 30, and 37 minutes at 1, 3 and 8 mg, respectively.

Treatment with placebo was associated with a one-minute reduction in mean MWT scores compared to baseline. Due to the magnitude and consistency of effect, at each dose level of ALKS 2680, the improvement compared to placebo was highly statistically significant, despite the relatively small number of patients.

Slide 22 shows the time course. ALKS 2680 showed clinically meaningful improvements in MWT from baseline at all doses tested and in all patients. At the 8 mg dose, patients maintained wakefulness for the full 40 min MWT duration up to 10 hours post-dose. MWT scores at 3 mg were comparable to 8 mg for the first 6 hours, and both 1 mg and 3 mg ALKS 2680 showed improved wakefulness for up to 8 hours post-dose.

The tolerability and efficacy profile of ALKS 2680 shown to date in NT1 is encouraging and informs our approach around dose selection, and our expectations as to tolerability and efficacy, in NT2. We've received some questions from investors regarding therapeutic index and potential dosing in NT2. Based on the pathology of NT2 and previous clinical data, we expect these patients to be less sensitive to orexin, requiring higher doses for efficacy and tolerating higher doses before observing limiting side effects. Based on our observed activity to date in NT1 and our modeling, we now believe that NT2 patients may only require 2 to 3 fold the ALKS 2680 NT1 dose. With a clear dose response and indication of therapeutic benefit at doses from 1 to 8 mg in NT1, and not having reached a maximum tolerated dose in patients or healthy volunteers, we are confident in our dosing flexibility and are currently enrolling NT2 patients in the study.

Concluding on slide 23, I'm pleased with the initial data generated from this innovative and efficiently designed phase 1 study, which support the key design objectives of the molecule. In less than a year, we have been able to establish a preliminary safety and tolerability profile of ALKS 2680 in healthy volunteers, demonstrate target engagement through EEG evaluations, establish a PK profile that supports once-daily administration with a target dose well below 10 mg in NT1 patients, and demonstrate significant wakefulness throughout the day.

We will continue to enroll the Phase 1b study in narcolepsy and IH patients and look forward to sharing those data. We are also in the process of finalizing the design of a phase 2 study which is planned to begin in the first half of 2024.

Now I will turn the call over to Rich.

**Richard Pops:**

Thank you.

Craig and his teams have accomplished a great deal in the past year to efficiently advance the ALKS 2680 program and generate the data presented this week at World Sleep. ALKS 2680 is an Alkermes designed and developed molecule. It is the product of expertise that Alkermes has accumulated in molecular design, medicinal chemistry, pharmacokinetic modeling, and neuroscience drug development. If the pharmacology of ALKS 2680 continues to be validated in the clinic, we believe it has the opportunity to be an important new mechanism in the treatment paradigm for patients with narcolepsy. And beyond that, it may provide the foundation to expand the biology of orexin agonism into additional potential disease areas -- some characterized by excessive daytime sleepiness, as well as others.

The data Craig summarized advance the ALKS 2680 development program past two important stage-gates: first, establishment of an initial safety and tolerability profile that supports further clinical development, and, second, demonstration of proof-of-concept through initial evaluations of efficacy using validated measures.

An important characteristic relating to both points is potency, expressed in the form of expected dose. Our modeling suggested, and the initial human data supported, a dose range for NT1 patients in between 1 and 8 mg. We believe that potency at these dose levels reduces the potential for off-target adverse events and, together with the tolerability profile observed to date, provides a wide potential therapeutic index to accommodate dosing in NT1 and NT2.

With this initial data set, we believe we have adequate information to complete the design of our phase 2 program. As we move into later-stage development, we will further establish the safety, tolerability and efficacy profile of ALKS 2680 through established regulatory endpoints as well as patient-reported outcomes, as we further explore the effects of modulating the orexin system.

So that is the ALKS 2680 program.

Shifting gears, we expect another transformational event to occur in the coming weeks with the planned separation of our oncology business into an independent, publicly-traded company called Mural Oncology. We are now in the final stages of implementing the separation, which has been a significant undertaking from an operational, logistical, legal and accounting perspective. As we prepare for the launch of Mural, it is paramount to us that Mural begins its journey as an independent company in a position of strength in terms of leadership, the ongoing clinical studies and financial resources.

Dr. Caroline Loew, the CEO designate of Mural, has recruited a talented management team and Board of Directors, and I am confident that their leadership will be a strategic asset. The potential registration-enabling studies for nemvaleukin in platinum-resistant ovarian cancer and mucosal melanoma are well underway and we have continued to focus on study enrollment and execution as we prepare for the separation. We believe the separation provides an opportunity to unlock value for both companies, create more optionality for shareholders, and position both companies for success.

Post-separation, Alkermes will emerge as a more profitable, pure-play neuroscience company with a clear strategy and well-defined opportunities for value-creation.

Taking a look back, 2023 has been a very productive year highlighted by the ongoing launch of LYBALVI, including initiation of the DTC campaign, strong enrollment and execution of our ongoing clinical studies in oncology and neuroscience, completion of the many workstreams to support the separation of the oncology business, and the successful outcomes of the Janssen arbitration and VIVITROL settlement. Each of these represents an important accomplishment in its own right, but collectively they transform the financial and growth profile of the company. We believe we are in a position to drive significant value for shareholders and look forward to sharing our progress with you.

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