Karuna Therapeutics, Inc. (NASDAQ:[**KRTX**](https://www.insidermonkey.com/insider-trading/company/karuna+therapeutics+inc/1771917/)) Q3 2023 Earnings Call Transcript November 5, 2023

**Operator:** Welcome to the Karuna Therapeutics Third Quarter 2023 Financial Results Conference Call. All participants are in a listen-only mode. Please note, this call is being recorded. I will now turn the call over to Alexis Smith, Head of Corporate Affairs and Investor Relations.

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**Alexis Smith :** Good morning, everyone, and thank you for joining the third quarter 2023 Financial Results Conference Call. I’m joined today by Bill Meury, President and Chief Executive Officer; and Jason Brown, Chief Financial Officer, who will begin our call prepared remarks. Andrew Miller, Founder and Chief Operating Officer; and Will Kane, Chief Commercial Officer, will join Bill and Jason for the Q&A portion of our call. Before we begin, I encourage everyone to visit the Investors page of our website at investors.karunatx.com to find our press release and presentation related to today’s call. Forward-looking statements related to our product development, regulatory and commercialization plans, our research activities and financial outlook may be presented during this call.

Please refer to today’s press release and our SEC filings for important risk factors that could cause our actual performance and results to differ materially from those expressed or implied in these forward-looking statements. And with that, I’ll hand it over to Bill.

**Bill Meury :** Thanks, Alexis. Good morning, everyone. I want to begin by thanking our R&D team and our external partners on a high-quality and timely NDA submission for KarXT for the treatment of schizophrenia. The team worked many long days and weekends over the past several months to write and submit our NDA. It was a major achievement for Karuna and represents the culmination of years of preclinical, clinical, CMC and regulatory work on KarXT detailed across several hundred thousand pages of information. Now the submission of course is just the first step in the NDA review process. There are several other important milestones and activities ahead including top line-data from the Phase 1b ABPM trial this month. We expect to hear back from the FDA on their filing decision later this month as well and we’re already preparing information for our day 120 safety update and site inspections among other things.

As we’ve talked about, we expect the standard review and therefore, a potential approval and launch in the second half of next year. As you know, the treatment of schizophrenia has been served by one class of medication for over 30 years and the potential approval of KarXT would change that for patients and their physicians. And I continue to believe this could be one of the most important product launches in biopharma in 2024-25. In terms of the prelaunch activities, they remain on track. We have the capabilities and the funding needed to optimize this program. We’ve built out our managed care access and MSL teams, we’re focused primarily on pre-approval scientific exchange meetings with payers, which started several weeks ago and on responding to medical information requests from psychiatrists and nurse practitioners.

Interest and anticipation for KarXT is very high in the community right now and we’ll continue to build over the next several quarters. Additionally, we have and will continue to present and publish new data from our emerging program this year and next year. Last month, we presented data from EMERGENT-3 at the European College of Neuropsychopharmacology meeting that highlighted KarXT’s differentiated tolerability profile demonstrated in the trial and potential to provide clinically meaningful symptom relief. The data includes new analysis on PANSS responders, which was the final prespecified secondary endpoint in the trial, and EMERGENT-3, nearly 60% of patients receiving KarXT achieved a 20% reduction of pain symptoms by week five at the end of the trial.

We also shared data on the PANSS motor symptom domain, including the PANSS Marder positive, disorganized thoughts, uncontrolled hostility, excitement and anxiety depression factors, where KarXT demonstrated statistically significant improvements from baseline to week five compared to placebo. On safety, we provided additional data to characterize the adverse events associated with KarXT and EMERGENT-3 were consistent with EMERGENT-1 and 2, the most common treatment-emergent adverse events were GI in nature, primarily occurred within the first two weeks of treatment, mild in severity and transient over time. Looking ahead, we’ll be sharing pooled efficacy and safety analysis from the EMERGENT-1, 2 and 3 trials as well as additional analysis on negative symptoms and adverse events at NEI in Colorado Springs and CNS Summit in Boston this month.

On the commercial front, preparations for the anticipated launch are on track too, including market research, sales force sizing and deployment and our peer-to-peer and consumer outreach programs. We have a team of people with a great deal of new product launch experience in neuroscience. They know what works and what doesn’t and are carefully evaluating all strategic and operational decisions to support the launch. Equally important to our regulatory achievements and pre-commercialization work for KarXT is the continued execution of our ongoing Phase 3 program, ARISE and ADEPT, which we believe reinforce the value proposition of KarXT as a potential treatment for psychosis-related conditions. For ARISE, site activation and improvement is ongoing with about 50 sites currently active across the United States and Europe.



As we maintain our target of sharing top line data in the second half of 2024, we continue to monitor site activation and enrollment rates very closely and manage factors that may impact enrollment on a day-to-day basis. Although there is no approved therapy for the adjunctive treatment of schizophrenia, the use of antipsychotics as combination treatment is seen in around 30% of patients despite the lack of clear pharmacological rationale and clinical evidence to support adjunctive use. Through ARISE, we hope to reinforce the unique weakness of KarXT’s differentiating clinical profile, and demonstrate that KarXT can be safely and effectively added on top of standard of care. I’m also pleased to share our ADEPT program evaluating KarXT for the treatment of psychosis and Alzheimer’s is fully underway following the initiation of ADEPT-2 and 3 in the third quarter.

We remain on track to share data from ADEPT-1 and 2, our relapse prevention and acute efficacy trials in 2025. As a reminder, the fundamental concept of KarXT originates from an Alzheimer’s trial, where xanomeline demonstrated promising therapeutic benefit in treating psychosis and related behavioral symptoms as well as cognition. Our ADEPT program is designed based on the insights from that initial strategy and our Phase 1b trial in healthy volunteers. And while our primary objective with ADEPT is to evaluate the efficacy and safety of KarXT in treating hallucinations and delusions associated with Alzheimer’s. We will also be collecting data, providing additional insights into the potential of KarXT in treating other prominent and clinically relevant symptoms of Alzheimer’s, including agitation, aggression and cognition.

The data from ADEPT may not only reinforce KarXT’s promise as the potential treatment for Alzheimer’s psychosis, but also help inform future developments with KarXT. Outside of KarXT, we’re also making headway in our early stage and discovery program, most notably with KAR-2618, a TRPC4/5 inhibitor that we have acquired from Goldfinch Bio at the start of this year. We plan to evaluate KAR-2618 for the treatment of major depressive disorder and anticipate initiating the Phase 1b clinical trial in 2024 with additional details such as trial design and refined timing to be shared early next year. Now on our earnings call earlier this year, I had highlighted three strategic and operational priorities that we set out to achieve in 2023. Those priorities were maximize the value of KarXT from a development perspective; two, expand our pipeline; and three, scale the operational capabilities of our company as we transition to a fully integrated R&D commercial organizations.

We’ve made excellent progress on these three fronts, which reflects the hard work and scale of our organization. With just a couple of months left in 2023, we look forward to finishing the year strong. With that, I’ll hand it over to Jason.

**Jason Brown :** Thank you, Bill. I’m pleased to be with you all today to share our third quarter financial results and to discuss our full year 2023 guidance. Q3 was another strong quarter for the company driven by continued progress across our ongoing KarXT Phase 3 programs, the submission of our NDA for KarXT, pre-commercialization efforts as well as significant growth across the organization. Total operating expenses for the third quarter were $136.2 million compared to $81.1 million for the same period in 2022. Operating expenses were slightly offset by $17 million in interest income, resulting in a net loss of $119.1 million. Research and development expenses for the third quarter were $104 million compared to $62 million for the prior year period.

The increase to $42 million was primarily driven by expenses related to our ongoing RXT clinical programs, increased employee head count and higher stock-based compensation. General and administrative expenses for the third quarter were $32.3 million compared to $19.1 million for the prior year period. The increase of $13.1 million was primarily driven by expenses related to our pre-commercialization efforts, increased employee head count and higher stock-based compensation. Cash, cash equivalents and investment securities totaled $1.3 billion as of September 30, 2023, compared to $1.1 billion at the end of 2022, providing us with a cash runway comfortably through 2026. The increase was due to our follow-on public offering in March of this year that resulted in a net proceeds of approximately $437 million.

Looking ahead at the rest of the year, we anticipate R&D to decrease in the fourth quarter relative to the third quarter and reiterate our guidance for the full year 2023, with total operating expense is expected to come in towards the top end of the range at around $470 million. Of that, we expect R&D and G&A expenses to be in the range of $355 million and $115 million, respectively. With the increase in R&D guidance being primarily driven by continued enrollment in our long-term safety trials by activation costs associated with the ADEPT program and costs related to our ambulatory blood pressure monitoring trial. I’ll now hand it back over to Bill.

**Bill Meury :** Thank you, Jason. With that, we can open the call to questions.Top of Form

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**Operator:** [Operator Instructions] Your first question is from the line of Yatin Suneja with Guggenheim.

**Yatin Suneja :** Hey, guys. Thank you for taking the question and congrats on all the progress. Just two quick ones for me, if I may. So the first one is with regard to the ARISE study. Could you maybe talk about your expectation? Would you expect the drug to behave similarly to the monotherapy in terms of the onset and depth of responses? And how should we think about the added tolerability impact. And then maybe on the pipeline front on 2618, you are prioritizing MDD. Could you maybe talk about the rationale going into MDD first over, let’s say, other anxiety disorder.

**Bill Meury :** Thank you, Yatin. Thank you for both questions. I’m going to turn it over to Andrew.

**Andrew Miller :** So with respect to the ARISE study from an expectations perspective, first, maybe to speak to efficacy. A reminder that the primary end point in the ARISE study, the total PANSS score is the same as the primary endpoint across EMERGENT 1, 2 and 3. So those do significantly inform our expectations about what we expect to see in the ARISE program. It’s a key difference with the ARISE program being we do expect the baseline severity of symptoms to be lower given that patients are being actively treated with existing antipsychotic medicines. Because of that, we expect a little less dynamic range and our expectation from a statistical powering perspective, is it more conservative, 4- to 5-point change on total PANSS in comparison to the 8 to 11-point change that we observed in EMERGENT program.

That still would meaningfully clear what we would consider clinically meaningful benefit in patients. And again, it’s all based on the same primary end point across the ARISE and EMERGENT programs. With respect to safety and overall tolerability, obviously, one of the things we’re most excited about with KarXT is the completely unique pharmacology, focused on the M1 and M4 muscarinic receptors. And when you look at the tolerability and safety profile, I think it’s very distinct in comparison to the adverse effects that are observed on current background standard of the care. So we continue to expect to see things consistent with the muscarinic pharmacology of KarXT and don’t expect meaningful overlap or for instance, worsening of background side effects associated with investors.

**Yatin Suneja :** And then you want to comment on 2618 at the preclinical evidence supporting utilization benefits?

**Andrew Miller :** I mean I think with 2618 and in general, TRPC4/5 as a therapeutic target for psychiatric illness and mental illness. I think there are a lot of interesting possibilities. I think that’s really the basis of your question, is that there’s evidence broadly to support both antidepressant and antilytic properties. Specifically, 2618 a molecule, but more broadly, TRPC4/5 as a target. I think our focus on MDD initially represents or representative of both our scientific confidence in that preclinical data, our ability to execute a study that we think will provide meaningful information specifically towards safety in a Phase 1b context, but also doing a study of patients that could provide some insight into the potential therapeutic benefits.

We certainly remain quite interested in a number of different anxiety disorders. Particularly, I would say generalizing anxiety disorder is something that we’re interested in evaluating with 2618 as well and look forward to being able to speak more of the details of that Phase 1b study here early next year as well as our longer-range plans for this program.

**Bill Meury :** And the only other thing I would add is that everything available today in MDD is effectively serotonergic and noradrenergic. And so we, of course, have some work to do to produce human efficacy data. But MDD is attractive because this would essentially be to the depression market, what in many respects, KarXT could be to the schizophrenia and the atypical market, which is a completely novel pharmacological approach, but we’ll know more at the end of ’24, early 2025.

**Yatin Suneja :** Thank you.

**Operator:** Your next question is from the line of Laura Chico with Wedbush Securities.

**Unidentified Analyst:** Hi. This is Ingrid on for Laura Chico. Wonder if you could talk a little bit about your expectations around real-world duration of treatment for KarXT cycling among therapies and even completely discontinuing therapies represents a hallmark of the schizophrenia space. How would you describe your base case expectations now that you’ve had longer-term experience with KarXT in clinical trials? Thank you.

**Bill Meury :** Yeah. I’ll make a few comments first, Ingrid and then turn it over to Will Kane, our Chief Commercial Officer. What I can tell you right now is that when you look at real-world experience with the second-generation atypicals, adherence rates are in the range of about only 50% to 60%, and the number of missed days of therapy each year is probably between 100 and 150 depending on which real-world observational study that you will look at. And so noncompliance is a real problem given the efficacy and safety experience some patients have that results in relapse, that results in ER visits and then, of course, hospitalizations and increased healthcare costs. We, of course, don’t have real-world experience yet. But we would expect that adherence with KarXT in the real-world setting could be higher, persistency could be longer and missed days of therapy lower. And I’ll just turn it over to Will to add a little bit.

**Will Kane :** Thanks, Bill. I’ll just echo some of the comments, Bill made, which is in the marketplace when we talk to clinicians and also to payers they see the potential for increased adherence is a real value add for KarXT. As Bill mentioned, there was the incremental increase from the typical to atypical, and given the mechanism and the clinical profile we’ve seen so far in the emergent program, there’s strong interest in seeing long-term data to realize the full potential of KarXT. And so when we don’t have real-world data, the data is indicating and signaling that there could be an opportunity here for increased adherence. And as we’ve talked about on M&A occasions, there’s a really high rate of non-adherence. Patients typically about two quarters of them of them or 75% will discontinue in the first 18 months, and that’s driven by a lack of either adequate efficacy or intolerability and KarXT may have the opportunity to really address both of those needs in the market.

**Bill Meury :** Thanks for the question.

**Operator:** Your next question is from the line of Myles Minter with William Blair.