Kymera Therapeutics Third Quarter 2025 Results Call | November 4, 2025

Operator:

Good day everyone. My name is Sophie, and I will be your conference operator today. At this time, I would like to welcome you to the Kymera Therapeutics Third Quarter 2025 Results Call. All lines have been placed on mute to prevent any background noise. After the speaker's remarks, there will be a question-and-answer session. If you would like to ask a question during this time and if you have joined via the webinar, please use the raise hand icon, which can be found at the bottom of your webinar application. If you have joined by phone, please dial star nine on your keypad to raise your hand. At this time, I would like to turn the call over to Justine Koenigsberg, Vice President of Investor Relations.

Justine Koenigsberg:

Good morning and welcome to Kymera's quarterly update.

Joining me this morning are Nello Mainolfi, Founder, President and CEO, Jared Gollob, our Chief Medical Officer and Bruce Jacobs, our Chief Financial Officer.

Following our prepared remarks, we will open the call to questions from our publishing analysts.

If you would like to ask a question, please use the raise hand icon, which can be found at the bottom of your meeting window. And to help us move efficiently through the Q&A session, we ask that you are ready to unmute your line when called on. In addition, we ask you please limit your question to one and a relevant follow-on to be sure we have enough time to address everyone's questions this morning.

Before we begin, I would like to remind you that today's discussion will include forward-looking statements about our future expectations, plans, and prospects. These statements are subject to risks and uncertainties that may cause actual results to differ materially from those projected. A description of these risks can be found in our most recent 10-Q filed with the SEC. Any forward-looking statements speak only as of today's date, and we assume no obligation to update any forward-looking statements made on today's call.

With that, I'd like to turn the call over to Nello.

Nello Mainolfi:

Thank you, Justine. And thanks everybody for joining us this morning.

Now in the final quarter of the year, as we reflect on 2025, I'm happy to say that our team has executed exceptionally well across all parts of our business, and we are very proud of all that we've accomplished this year. We are committed to building a global biopharmaceutical company and have established a strong foundation that will serve us well as we scale our organization and continue to advance our industry-leading oral immunology pipeline.

As shown on this slide, I'd like to highlight a few of our key achievements this year that positions us well for important future milestones.

In less than two years since unveiling our STAT6 program, we have demonstrated exceptional progress in advancing our first-in-class STAT6 degrader, KT-621. To recap:

- We completed our healthy volunteer study ahead of schedule with impressive results.
- We enrolled and completed dosing in the Phase 1b trial in AD patients, with data coming in December.
- We Initiated our first of two Phase 2b trials, BroADen2 in AD, and we're on track to start the BREADTH Phase 2b asthma trial in the first quarter of 2026.
- We were also featured in two recent late breaking presentations which have helped us maintain high visibility with the medical and scientific communities where there continues to be strong interest in oral medicines with potential for biologics-like activity.

Beyond STAT6, we unveiled our IRF5 program this spring and presented the robust preclinical data at the American College of Rheumatology annual meeting, just recently. We have also completed the KT-579 IND enabling studies and remain on track to initiate the first clinical trial in healthy volunteers early in 2026. In addition to IRF5, we continue to advance our earlier stage, undisclosed immunology pipeline, and our goal remains to address many of the major immunology indications with oral medicines. Importantly, we believe the synergies across our pipeline provide multiple development opportunities for broad patient populations.

We also entered into a new partnership with Gilead outside of immunology. Gilead is an ideal partner to drive forward our CDK2 oncology molecular glue program, which we believe has broad potential in breast cancer and other solid tumors.

In summary, it's been a very busy year and a successful one, and we look forward to finishing the year strong as we advance our pipeline towards more and more important milestones.

More broadly, we've built what I believe is one of the strongest oral Immunology pipelines in the industry, where we're well positioned to deliver novel oral treatment options for patients with highly prevalent immuno-inflammatory diseases. Several years ago, we made a deliberate strategic shift to focus our R&D efforts toward the significant opportunities in immunology. And the reason is quite simple. Within Immunology, many pathways have been validated with upstream biologics. Traditional small molecule inhibitors are not able to block the signaling pathways as effectively as biologics given their direct correlation between PK and PD and the need of high drug exposures. As a result of the power of protein degradation, we can now selectively remove disease-causing proteins through a catalytic mechanism and can block pathways completely, which we've consistently demonstrated across all of our programs. This allows for the potential of oral drugs with biologics-like activity for the first time in our industry, and our first-in-class pipeline is a testament to this strategy.

If we look specifically at our STAT6 program, KT-621 exemplifies this approach. There is a tremendous opportunity for a convenient, safe and effective oral pill in highly prevalent Type 2 diseases like atopic dermatitis, asthma, COPD, EoE and others. Despite the large size of the patient populations, the penetration of other systemic advanced therapies, like injectable biologics, is actually quite low. This creates a significant opportunity for safe and effective oral medicines which we believe would have potential to change the quality of life for many patients and families around the world.

We have moved our STAT6 program at a rapid pace from preclinical to IND to initial clinical proof of concept and now we're embarked on our first global Phase 2b trials. In fact, we filed our IND in September 2024, and by the fourth quarter of 2025, we've already launched our first Phase 2b study. This progress is a strong testament to the speed, focus, and executional excellence of our team in driving this program forward.

Looking back at the KT-621 Phase 1 healthy volunteer study, we demonstrated that at very low doses, we can degrade STAT6 fully and block Th2 disease-relevant cytokines in healthy volunteers as effectively as upstream biologics, and in a well-tolerated manner.

We are moving quickly toward completion of the BroADen Phase 1b trial, which we initiated in the spring. To remind you, the trial was designed to achieve three important goals.

To confirm robust degradation in the blood and skin and understand the translation from healthy volunteers to AD patients;

To allow us to refine the Phase 2b doses based on that translation; and

To demonstrate that robust STAT6 degradation in AD patients can impact biomarkers and clinical endpoints similar to upstream biologics, specifically dupilumab.

Given that the trial is fully enrolled and we plan to share the data next month, I wanted to use this call, one last time, to reiterate the expectations we're setting heading into the study across the four key dimensions we are evaluating KT-621: degradation, safety, biomarkers and clinical activity:

With respect to STAT6 degradation, the goal is to translate in AD patients the robust degradation of STAT6 in blood and skin that we have seen in the Phase 1 healthy volunteer study.

The safety profile is paramount, and we hope to continue to see a safety profile in line with what we have seen in both healthy volunteers as well as our preclinical studies.

With respect to biomarkers, we plan to look in both blood and skin.

In blood, we have highlighted TARC as the most relevant biomarker at the 4-week time point. After achieving up to a median reduction of 37% of TARC in healthy volunteers and given atopic dermatitis patients generally have higher baseline TARC levels, our expectation is to show a meaningfully more robust TARC reduction.

As a point of reference, in published dupilumab studies where baseline TARC levels were much higher than healthy volunteers, the reduction was in the range of 70%-80% at 4 weeks, which is the bar we set for KT-621 assuming generally comparable baseline levels.

In skin, we also plan to assess KT-621's impact on skin transcriptomics, which we had not assessed in our healthy volunteer study. There, we anticipated changes in downstream genes that aligns with the expected biological effects of this pathway modulation.

And finally, in terms of clinical endpoints, we went into the study with a robust body of evidence in all of our experiments demonstrating that KT-621 blocks IL-4 and 13 as well as dupilumab and this has resulted in comparable downstream pathway effects in both *in vitro* and *in vivo* studies. As a result, we entered the BROADEN study expecting clinical activity of KT-621 to be in the range of what dupi delivered at 4 weeks in its published studies, including on both EASI score and itch, with all the caveats of small N's and the lack of a placebo arm.

I hope that this is helpful as we approach the data readout next month. Given that we have quite a bit of investor activities planned this month, please understand we will refer back to these key objectives and reserve any additional commentary for the final data presentation in December.

So, before I hand the call back to Jared, I wanted to take a moment to welcome Brian Adams, our new Chief Legal Officer, to Kymera. He is a seasoned life sciences executive with deep industry experience, bringing more than two decades of experience across legal and compliance, corporate development, strategic planning, and governance. We're thrilled to have

him join our team as we enter this next phase of our growth and look forward to his contributions as we continue our efforts to building a fully integrated commercial company.

So, to wrap up, as I said at the onset of the call, this has been a year of exceptionally strong execution, and we're well positioned to continue advancing all aspects of our pipeline as we head into 2026. I'm confident that through our expertise, scientific rigor, and focused execution we are building one of the most exciting immunology portfolios in this industry.

Let me pause here and turn the discussion over to Jared, who will provide us an update on the pipeline including additional color on the newly initiated atopic dermatitis study. Jared?

Jared Gollob:

Thanks, Nello.

We have made significant progress with KT-621, our STAT6 degrader, and I'm happy to share the advancements we are making in the clinic with you this morning.

As Nello described, we see this as a transformative opportunity to develop an oral therapy that delivers biologics-like efficacy without the limitations of injectables.

KT-621 is the first and, we believe, only STAT6-directed oral medicine in the clinic. It has the potential to positively impact the more than 130 million people around the world living with Type 2 diseases, considering all the indications where dupilumab is approved today.

Our first development indication is atopic dermatitis, or AD, a common but complex dermatologic condition with a significant unmet medical need. This is a chronic, inflammatory skin disorder, more commonly referred to as eczema, that manifests as inflamed, itchy, and often painful patches on the skin. These lesions can appear anywhere on the body and range widely in severity from mild irritation to debilitating, full-body inflammation.

One of the most burdensome aspects of this disease is the persistent itch. It's not just a nuisance, it's a hallmark symptom that can severely impact quality of life by disrupting sleep, daily activities, and overall well-being.

While there are several treatments available today, they have limitations, forcing patients to make tradeoffs.

Antibody-based injected therapies, like dupilumab, have made a real difference for many patients, providing a well-tolerated and safe therapeutic option, but it's not a solution for everyone. For starters, access can be very limited and is a challenge for many patients. For those

who are prescribed these drugs, it can be inconvenient or a painful route of administration, with compliance impacted by lack of tolerance of injection site reactions or phobia of needles. And there are also issues with cold storage requirements and immunogenicity risk. In fact, in an industry survey, 75% of patients taking biologics said that they would switch to orals with an equivalent profile. There are some oral options, such as JAK inhibitors, that offer an effective oral alternative. However, they come with significant safety concerns, including box warnings, that limit their use, especially in long-term disease management.

Given this important unmet need, coupled with the strong preclinical and clinical profile of KT-621 in healthy volunteers, we have developed an accelerated clinical development strategy including conducting a small Phase 1b biomarker-focused trial in moderate to severe atopic dermatitis patients that we initiated earlier this year.

The key aim of the 28-day BroADen study is to show that robust STAT6 degradation in blood and skin lesions by KT-621 has a dupilumab-like effect on multiple Th2 biomarkers in the blood and skin. We will also assess KT-621's effect on clinical endpoints, such as EASI and pruritus NRS.

The team has worked very hard to advance this program and, in line with expectations, we completed enrollment in the study last month and dosing is now complete. The final patients are completing follow-up, and we will collect and evaluate the rest of the data and report results in December.

As we have said, this Phase 1b study was not gating to the start of the parallel Phase 2b dose range finding trials in AD and asthma which in turn are designed to enable subsequent Phase 3 registrational studies across multiple indications. This quarter, we initiated BROADEN2, our Phase 2b AD study, a global, randomized, double-blind, placebo-controlled trial to evaluate KT-621 in approximately 200 patients with moderate to severe atopic dermatitis.

This study is designed to evaluate three different doses of KT-621 over a 16-week treatment period, compared to placebo. Patients from the study have the opportunity to participate in a 52-week open label extension period after completion of the trial, which will contribute to building the long-term safety database we'll need to support eventual regulatory filings and is also an additional incentive for patient recruitment to the trial.

Eligibility criteria to ensure we're recruiting patients with moderate to severe AD include an EASI score of at least 16, at least 10% of body surface area affected, and an average weekly Pruritis NRS score of at least 4. While prior use of biologics is permitted if treatment was not discontinued for lack of response and following a study-defined washout period, we expect to enroll a substantial number of systemic treatment-naive patients given the attractiveness of the ease and convenience of a once daily oral treatment option.

The primary endpoint is the percent change from baseline in EASI score at Week 16. Secondary endpoints will evaluate a range of additional safety and efficacy measures, including but not limited to the proportion of patients achieving EASI-50, EASI-75, a validated Investigator Global Assessment score of 0 to 1, and at least a 4-point improvement in Peak Pruritus NRS. We expect top-line results from the Phase 2b study will be available by mid-2027.

In addition to atopic dermatitis, we plan to initiate the BREADTH Phase 2b study in asthma in the first quarter of 2026. We'll share more information on the trial design next year, when we get closer to initiation.

Beyond the STAT6 program, we have completed IND-enabling studies with KT-579, our IRF5 degrader, which we plan to advance into a Phase 1 healthy volunteer study early next year with data expected in 2026 as well. Last month, we shared incremental updates in two posters at the ACR meeting in Chicago. In several preclinical efficacy models of lupus and RA, KT-579 was generally more efficacious than clinically active or marketed small molecule inhibitors and injectable biologics, phenocopying IRF5 knockout studies. The compelling preclinical data we have generated showcase that targeting IRF5 can lead to correction of immune dysregulation across multiple disease pathologies while generally sparing normal cells. We continue to be excited about this opportunity and look forward to moving it into the clinic soon.

I'll pause here and turn the discussion to Bruce to review our third quarter financial results. Bruce?

Bruce Jacobs:

Thanks, Jared.

As I walk through the third quarter results, please reference the tables found in today’s press release and 10-Q, which was filed this morning.

Revenue in the third quarter of 2025 was $2.8 million, all of which was attributable to our collaboration with Gilead.

With respect to operating expenses, R&D for the quarter was $74.1 million. Of that, approximately $8.4 million represented noncash stock-based compensation. The adjusted cash R&D spend of $65.7 million, which excludes that stock-based comp, reflects a 7% decrease from the comparable amount in the second quarter of 2025.

On the G&A side, our spending for the quarter was $17.3 million dollars, of which $7.4 million was noncash stock-based comp. The adjusted cash G&A spend of $9.9 million, again, excluding

that stock-based comp, reflects a 3% decrease from the comparable amount in the second quarter.

Overall, adjusted operating expenses were down slightly from the prior sequential quarter.

We ended September with a cash balance of $978.7 million, providing a cash runway into the second half of 2028. This runway allows us to complete both KT-621 Phase 2b trials in AD and asthma, cover start-up costs and initial Phase 3 activities for the STAT6 program, advance KT-579 through initial POC testing, and advance our research pipeline as we scale and grow Kymera.

Just a quick reminder, our runway collaborations, calculations I should say, exclude any unearned milestones from our collaborations with Sanofi and Gilead. Regarding Sanofi, we expect they will advance KT-485 into Phase 1 testing in 2026, which would trigger a development milestone payable to Kymera. As for the Gilead collaboration, upon exercising its option for a CDK2 glue we are entitled to a milestone payment. As previously announced at the time of signing the Gilead collaboration agreement, we are eligible to receive a total of $85 million in upfront and option payments, with approximately half of this already received as the upfront payment in the last quarter. We look forward to the continued progress of both the IRAK4 and CDK2 partnered programs.

With that, we'll pause here so we can convene in our main conference room and open the call for questions. Thank you.

Moderator:

Thank you. At this time, if you would like to ask a question, please click on the raise hand button, which can be found at the black bar at the bottom of your screen. If you have joined by phone, please dial *9 on your keypad to raise your hand. When it is your turn, you'll receive a message on your screen inviting you to join as a panelist. Please accept and wait until you are promoted to panelist. Please unmute your audio, turn on your camera, and ask your question. As a reminder, we are allowing analysts one question and one follow-up related question today. We'll now pause a moment to allow this queue to assemble.

Moderator:

Your first question comes from Geoff Meacham, Citi. Please unmute and ask your question.

Geoff Meacham:

Okay, great. Hey, guys. Thank you very much. I just had a couple questions. So the first one is, when you look at the upcoming data for KT-621, maybe just highlight, Nello, what are the key characteristics that could enable it to potentially show differential efficacy versus dupilumab. At

relatively early time points, I think that's probably one of the bigger points of uncertainty with investors.

And then the second question is, when you look at the two doses of the BroADen study, or the three doses, is the expectation that the lower one maybe has a lower impact on degradation and therefore is sub-therapeutic? Or is it to test the upper end of where you'd like to be from a safety and tolerability? I'm just trying to get a sense for the selection of the doses, and kind of how you would frame that out for what would be the ideal result.

Nello:

Great. Thanks, Geoff, for the question. So on the first one, let me just take a step back. So, in all the work that we've done with our STAT6 program for multiple years now, we've been working on this program for a very long time. We were able to demonstrate I think convincingly in all the preclinical studies that when you degrade STAT6, you're able to block IL-4 and IL-13 signaling, as well as an upstream biologics, whether it's an IL-4 receptor blocking a drug like Dupixent, or even an IL-13 drug. So generally, we're actually the only oral drug that is able to block IL-4 and 13 as well as upstream biologics.

In all the studies that we've run, again, preclinically, as I said a few minutes ago, both in vitro and in vivo, we've seen comparable activity. And I think this speaks to the biology of the pathway. Whether you block the receptor or you block the specific transcription factor for the receptor, you see the same biology.

So, the reason why we say the opportunity here is to have dupilumab in a pill-like profile, is not because it's actually what we hope to see, obviously we hope to see that, but it's because it's the activity of the biology that we've seen so far. So, as a data-driven company, as we are, we're reporting the observation of, so far, we've seen dupi-like activity.

In our Phase 1 healthy volunteer study, where we measured, as you remember, biomarkers in blood in healthy volunteers, we were able to show also in those biomarkers that we were generally comparable, and some would say even numerically superior to dupilumab. So for me, it's really hard to say KT- 621 is going to be better than dupilumab or worse than dupilumab. All we've seen so far that we're generally blocking the pathway the same way. Hence, that's where the expectations are set.

Now, as a data-driven drug development company with, I think, astute people in the company, we're very keen to see how the two profiles will evolve and where they will differentiate. We're talking about obviously an injectable biologic versus small molecule degrader. So, you will see probably small differences or larger differences here and there, a priori, it's very difficult for us to set the expectation one way or the other. I would be probably the happiest CEO in the world if we're able to deliver a dupi-like profile.

Going to your second question, I think I understand what you're saying, what you were asking, but maybe not. So, you can correct me if I got it wrong. So, maybe the way that I'm going to answer your question is, we selected two doses for the Phase 1b study, because we wanted to really understand well what was the translation of healthy volunteer degradation profile into patients, to then have high level of confidence in selecting the three doses for the Phase 2b. The only thing I'm going to say right now is that the two doses of the Phase 1b, as well as the three doses for the Phase 2b, are all within the doses that we studied in the healthy volunteer study. And generally, our approach for the Phase 2b is to evaluate a range in which we see maximum pharmacology, and at the top dose, or some would call a super pharmacologic, and then in the bottom dose, a dose that reaches less than the optimal pharmacology. And then obviously, a dose in between. That's the general philosophy without going into details.

Geoff Meacham:

Thank you very much, yep.

Moderator:

Thank you. Your next question comes from the line of Marc Frahm, TD Cowen. Please unmute and ask your question.

Marc Frahm:

Thanks for taking my questions. Maybe just on the Phase 1b, Nello in your comments you mentioned the target of 70 to 80% TARC reduction, but with that caveat of assuming similar baseline characteristics. Now that you've enrolled the patients with a group of 10 per dose level, there's always some chance that you end up with a little bit of a skewed population relative to the comparators. Just anything you'd highlight there based on the patients that have actually enrolled that might be a little bit different than the historical Dupixent comparators. And then I'll probably have a follow-up.

Nello:

Yeah. No, Marc, that's a great question. So let me clarify. So, there is two aspects of this trial. One is the baseline, let's say the baseline EASI of patients. And then I think what I was referring to back a few minutes ago was the baseline TARC levels. So, I think if you study dupilumab TARC reduction over both the AD study, but actually if you study over all the other studies that were run in other indications, whether it's chronic rhinosinusitis, asthma, EoE, et cetera, you see that there is a clear relationship between baseline level of TARC in patients, and reduction of TARC. And so that's what I was referring to, when I'm talking about baseline level of TARC, baseline

levels I was referring to the TARC baseline levels. And obviously, I'm not going to comment about what the baselines of our study are, but obviously we'll share the data when the time is right.

Then there is another element, which I want to clarify, then there is the EASI baseline levels. And I think what we've said in the past, as we've seen generally when dupilumab was developed, it was the first systemic drug for atopic dermatitis. And so if you look at those studies, the baseline EASI were in the high 20s, low 30s. If you look at studies from all companies in the past five years or so, you see that the baseline EASI has shifted down in the, let's call it, mid-20s. That's mostly because the patient population that were accessing to these trials in the sites that most companies go to obviously has changed, given that these sites in these countries and these regions have access to dupilumab.

So generally, the most severe patients are on systemic biologics. Some are not, but generally the mean number has come down a bit. And that's what we're observing. And so that's another element to the whole study and the outcome of the study. But I just want to separate the point that I was making before, were on TARC baseline levels, not necessarily on the EASI baseline level.

Marc Frahm:

Okay. And should we expect that same trend to lower EASI scores? It should apply here, but does that have an impact on likely TARC levels as well, do you think?

Nello:

I think that's something that we'll discuss when we release the data. I think we understand really well, obviously the level of TARC baseline in healthy volunteers, where we've seen reduction in the mid to high 30s in many patients on our studies, in the healthy volunteers. And we show that also dupilumab when baseline levels were in the range of healthy volunteer had similar reduction. I think again, as I've said, if you look at other studies, dupilumab level, you see a correlation between baseline level and percent reduction of TARC. And so I think that's the observation that we're sharing, looking at those studies. I don't want to preview our study because, as I mentioned a few minutes ago, I don't think it would be productive to preview some data here versus December.

Marc Frahm:

Okay, thank you.

Moderator:

Your next question, it comes from the line of Brian Abrahams, RBC. Please unmute and ask your question.

Brian Abrahams:

Hey, guys. Thanks so much for taking my question and congratulations on all the progress. I'm wondering how are you guys thinking now that it's been initiated about the powering overall for the Phase 2b AD study, just considering the population you expect to enroll, the mix of biologics and experienced and naive patients, and your expectations for effect size. And then just as a follow-up, it sounds like you're thinking about maybe different doses for asthma and respiratory diseases versus dermatological diseases. Just wondering if you could elaborate a little bit more about what you think are the important considerations around that. Thanks.

Nello:

Jared, do you want to take it?

Jared:

Sure. Yeah, I mean, we can't give specifics around powering for the Phase 2b. What we can say is, and we have stated that the N for that study is going to be approximately 200 with there being four arms, three drug, one placebo. So, we look very carefully at what the expectations are with the patterns have been in the past with regard to EASI responses, and pruritus responses, et cetera, and that's all gone into calculating what sort of ends we need to make sure that the study is adequately powered. So, we've been very careful in the design of the study to make sure that we are powered to show that desired effect relative to placebo.

Another important aim of the study obviously is to be able to look across the three different doses to see if we can discern any sort of a dose response. So the study is powered to enable us to do all of those things.

Nello:

The doses between AD and asthma.

Jared:

Oh, the dose between AD and asthma. So right now, so I think what we've guided is that our plan is to, in the Phase 2b, to use the same doses for both AD and asthma across both Phase 2b studies.

Nello:

And then maybe just to add, then the Phase 3 doses, or dose that will be used for AD Phase 3 and asthma Phase 3, might be different based on the dose ranging. To be honest, our expectation is that it will not be different, and we will use one dose for all studies. But that's why we're running different dose ranging in different diseases with different target tissues, so that we actually understand what the right dose will be.

Brian Abrahams:

Got it. That's really helpful. Thanks so much.

Nello:

Thank you.

Jared:

Thanks.

Moderator:

Your next question comes from Brian Cheng, JP Morgan. If you'd like to unmute yourself and ask your question.

Brian Cheng:

Hey, guys, thanks for taking our questions this morning. Some of the color you're providing here for the December readout is pretty much in line with what you already messaged. But I'm just curious, just given the gap between the time you selected your three doses for the Phase 2bs, and when Phase 1b finished enrollment around early October, what could be additive to what you already know in the December readout? Or do you think the data is most likely going to be in line with the data that you had already seen when you pick the three doses and have a follow-up?

Nello:

Well, I like to maybe clarify. I think what we said before is the same thing that we've been saying for nine or 10 months, but that's maybe just my small additional color. So, I just want to clarify. When we selected the doses for the Phase 2b, was actually a few months before October, right? We started the study recently, the Phase 2b study, but in order to submit the protocol and do startup activities, you had to actually have chosen the doses much earlier. And I think I've said this many times, I believe publicly, that when we selected the doses, we had visibility into partial data for both doses, for both the first dose in the 1b and less, but still some data from

the second dose in the Phase 1b. And again, we did not have access to the totality of the data, but because we're focused mostly on the translation of degradation and obviously safety, which is understood, we had enough information to make the right selection for the Phase 2b doses.

Brian Cheng:

Thanks, Nello. In the prepared remarks, in the BROADEN2 trial design, I think you mentioned that you expect a substantial number of patients to be naive to advance therapy. I'm just curious, what's the driver behind that and how should we take that into account as the investors think about comparing the BROADEN2 future data against other benchmark?

Nello:

Yeah, so I'll start. Jared, please jump in. The reason why we believe that will be the case is multifold, but I will start with, we believe KT-621 and our STAT6 program is, the whole value proposition is to expand patient access to advanced systemic therapy. The penetration of these advanced biologics in moderate to severe patients is less than 10%. Some companies claim it to be more than 10%. Maybe we align on, let's say, 10%, so we don't have to argue with other companies. The majority of the patients do not have access to advanced systemic therapy. That's where we are coming from. Then another part, which we've discussed as well, is patients that have gone on to systemic therapies that have failed pathway systemic therapy, IL-4, IL-13, JAKs, will not come onto our study. They will have to have responded to those therapy, then decided not to continue and then jump on our 621 study.

For those two main reasons, and also I would say for the experience that we had in the Phase 1b, we believe the majority of patients would be naive, and I would also add, hopefully I will not be proven wrong, that we don't believe there'll be issue out there finding naive patients because those patients are in dire need of an active systemic oral safe therapy.

Jared:

The only thing I would add would be just as a reminder that this is a global study. We're running this study in North America, Europe, Australia, and Japan, with the majority of sites actually being ex-US. Ex-US, in particular, they're going to be a number of patients who don't have access to dupi. And so that's another reason why we expect substantial proportion of patients on 2b to be dupi naive.

Brian Cheng:

Thanks for the color. Thank you.

Jared:

Thanks, Brian.

Moderator:

Your next question comes from the line of Mayank Mamtani. B. Riley, if you'd like to unmute yourself and ask your question.

Mayank Mamtani:

Yes. Good morning, team. Thanks for taking our questions and congrats on the progress. Could you give us a little bit more detail on the asthma BREADTH, I think you're calling it, trial considerations, in terms of, if you're looking at a 12- or 24-week FEV1 endpoint or a longer duration exacerbation. You could be looking at both, but just wonder in terms of which is your primary endpoint. And then also curious about the kind of patients you're thinking to enroll there and the allowance of background therapies. And obviously the question is around timelines for data readout for the asthma and atopic derm, will they be stacked together in 2027? And then I have a quick follow-up.

Nello:

Yeah, no, thank you for the question. Unfortunately, as we've said, we're going to talk more about the Phase 2b BREADTH study when we're in the startup mode, when we're close to dosing our first patient. Give us a few more weeks and then we'll provide all the color that you're asking for. Why don't you ask the follow-up so that at least you get a question.

Mayank Mamtani:

And maybe just to talk a little bit beyond 621 and about your pipeline beyond that. Just on the 579, could you maybe give us some color on what the initial targeted indications would be, just given the broader inflammation cascade that you're targeting there? Thanks for taking the questions.

Nello:

Yeah, maybe just high level. Thanks for asking about IRF5. This is a program that I think has mostly been unparalleled in the industry where you have a highly validated, genetically validated transcription factor that has been, I think, the object of many drug development efforts in the biopharma industry for a decade or so. But has maintained, has remained elusive where Kymera has that solution using targeted protein degradation. So if you look at human genetics, the top four places where one would go directly are generally lupus, SLE, and other subcategories of this disease. Some other interferon-related pathologies, RA, IBD. Those are where human genetics point to, our preclinical data point to. I think one more closer to the

Phase 1 study, we'll be able to share more about our development plans. Jared, anything you want to add?

Jared:

No.

Nello:

Thank you.

Moderator:

Your next question comes from the line of Sudan Loganathan from Stephens. Please unmute and ask your question.

Sudan Loganathan:

Hi, good morning, Kymera team. Thank you for taking my question. Looking back at the healthy volunteer data for KT-621, I noticed that the median percent change in the serum TARC and the IGE were similar to that of dupilumab healthy volunteer outcomes for those same levels when on treatment. There was a noticeable rebound higher, obviously on these levels when the patients were off of KT-621, as you showed. My question is, how important is the durability for the AD and asthma patient's quality of life outcomes? And will KT-621's daily oral dosing regimen make up for any deficiencies and maybe a durability outcomes that it could have compare to dupi? And does dupilumab mode of administration and systemic effects just inherently lend to a more durable outcome?

Nello:

It's a great question. I will answer part of it and then I'll let Jared also speak to part of all of it. The beauty about our drug is that it's a once a day oral that allows you to block IL4/IL13 continuously at steady state. The beauty of our drug is that you can stop and start when you want, if needed, without long wash-out period. The beauty about a once-a-day oral drug is that as long as you continue to take the drug once a day orally, you will see profound effects. Or at least the effect that the biology, the underlying biology will have.

I don't believe that if these drugs are taken as prescribed, obviously we're still very early to compare to dupilumab, that you have more or less duration of the effect. The only main difference that I will say between an injectable biologic and a once a day oral degrader, not small molecule inhibitor, is that the once a day oral degraders allow you to have steady state complete pathway blockade. I believe with dupilumab a couple of days before your next dose,

you're not maximizing the pharmacology as much. So you might actually have less pathway blockade, continuous pathway blockade, than a once-a-day oral degrader. What would that mean from a therapeutic perspective? Obviously, time will tell and studies will tell.

Jared:

Yeah. And maybe coming back to your comment around the Phase 1a. Just to clarify, patients were on the MAD portion were getting 14 daily doses. And so when we look at the effect on TARC and Eotaxin-3 in particular, that suppression or inhibition was seen throughout the entire 14-day dosing period. In fact, if you looked at Day 7 versus day 14, levels were actually continuing to go down, TARC and Eotaxin-3, between Day 7 and 14, which suggested that if we had continued dosing beyond Day 14, we might've seen more suppression. So there was no recovery of TARC and Eotaxin-3 until dosing was stopped after Day 14, and then you see a gradual recovery. So that just speaks to what Nello was referring to in terms of the durability of the effect as evidenced by, even in healthy volunteers, a durable effect on those biomarkers. Thanks.

Nello:

Thank you.

Sudan Loganathan:

Thank you. Thanks.

Moderator:

Thank you. Due to time restraints, we are now limiting analysts to one question only. Your next question will come from Andy Chen, Wolfe Research. If you'd like to unmute yourself and ask your question.

Brandon:

Hey, this is Brandon on for Andy, and thank you for taking our question. Within BROADEN2, are you doing anything to control the rising trend of placebo that we're seeing in atopic dermatitis where recent trials have seen a higher placebo response?

Nello:

Thanks for the question. I just want to answer the first part and then Jared will address it. I think that's an important point. I think, as I was speaking earlier, I think with a drifting of patient, with EASI shifting from, let's say, early 30s to mid 20s, I think it's almost physiological to have seen an

increase of the placebo rates. I think though there are ways in which one can minimize the effect. And maybe Jared, you can speak to it.

Jared:

Sure. Yeah. I think, as far as we see it, I think this is based on the general learning from prior studies. There are really three main things that one can do to try to limit that placebo rate. One is making sure that you have the right protocol design and site selection so that you're making sure you actually have patients with atopic dermatitis, not other skin diagnoses. And that you make sure you have moderate to severe patients, that you're not somehow also getting mild patients, the milder patients. The more mild patients you have, who should not really be enrolled in these studies, but if they are enrolled are going to have a contribution to placebo rate. A second important thing is to select very experienced sites because you want the raters, the people who are assessing the endpoints that have the right expertise, the right derm expertise here for AD.

And you also want to have the proper training of those raters to make sure they're able to assess EASI, for example, consistently and accurately. And then finally, it's really important that there be close sponsor oversight of the sites involved and also the CRO that's helping to execute on the study. That oversight is really of study conduct, and the sponsor has to really be all over study conduct. I think all of those elements combined I think are important in helping to mitigate placebo rate, and those are all things that we're addressing in our study.

Brandon:

Thank you.

Moderator:

Your next question comes from Kripa Devarakonda, Truist. If you'd like to unmute yourself and ask a question.

Kripa Devarakonda:

Hey guys, can you hear me?

Nello:

Yep.

Kripa Devarakonda:

Yeah. Thank you so much for taking my question. I was actually wondering how you think about the evolution of the competitive landscape for 621. I know you guys are significantly advanced in terms of the clinical development. There are competitors, whether you talk about degraders or some inhibitors. But based on what you've seen, how important is the fact that you are ahead in development versus any potential areas of differentiation? And where does the next gen STAT6 degrader fit into this context? Thank you.

Nello:

Thanks, Kripa. Obviously, yes, we're aware of other companies that I think we've enabled with our amazing data over the past couple of years, which is obviously always great to see, at least from an industry perspective. First, let me start with, this is not just about being first. I think this is about being first and best because that's what is going to almost guarantee commercial success. You're ahead of the competition, which is important, but more importantly, you have a drug that is going to be extremely difficult, if not impossible, to do better than. And that's what KT-621 is. It's a drug that is exceptionally potent, as we've seen, exceptionally well tolerated with a profile that we believe would allow us to go in any potential indications of patients with Th2 diseases. I think others will have to talk about their differentiation versus KT-621.

I'm not familiar with many of the other programs because there haven't been any publications on presentations with actual data. What I will say, going on record here, is I believe a small molecule inhibitor of STAT6 is impossible to reach the level of pharmacological effect that our degrader will have. Mostly because will not be able to block this pathway 24/7 almost completely or completely as we do. And we believe that that's required to have biologics like activity. On the other, obviously degrader programs, again, I don't know enough. The important thing here is that we have confidence in our drug. We're years ahead of competitors. And so our team mandate here, including us around the table, is to execute flawlessly in the next few years so that we can accomplish the commercial success that will make KT-621 double-digit billion dollar drug in the Th2 space.

Kripa Devarakonda:

Great. Thank you so much.

Moderator:

Thank you. Your next question comes from Jeff Jones, Oppenheimer. If you'd like to go ahead and ask your question.

Jeff Jones:

Good morning guys, and thanks for taking the question. We've been talking about TARC, Eotaxin, and some of the other critical biomarkers for the STAT6 program. Can you comment on key biomarkers we should be focusing on for the IRF5 program when we see that data? And should we be expecting healthy volunteer data in 2026?

Nello:

Yes. Jeff, you always ask very methodical questions. I love it. Yes, we expect to have Phase 1data from 579 in 2026, next year. It's a bit early to speak to the biomarkers, but as you know us, as you do know as well, we tend to run Phase 1 healthy volunteer study that are quite rich in terms of information. As we get closer to the start of the study, we'll share more about our biomarker strategy.

Jeff Jones:

Thanks guys.

Nello:

Thanks.

Moderator:

Thank you. Your next question comes from the line of Jeet Mukherjee, BTIG. If you'd like to ask your question.

Jeet Mukherjee:

Great. Thanks for taking my question. You folks have spoken at length about the niche and the opportunity for KT-621 in the atopic derm space, but could you just elaborate a bit further on how you see it fitting within the asthma landscape? Thank you.

Nello:

Yeah, I'll start with actually, there's a more fundamental issue I think in the asthma space. And I'll let Jared speak to the medical part of it. I just want to talk strategically. So Th2 asthma, eosinophilic asthma, which obviously we expect this drug to address, just to level set, is a disease that start very early in life. And actually it turns out that if you're not able to impact the disease until or before your lung fully develops, you're actually going to have reduced lung function for the rest of your life. And children, young adults, are on therapies that do not address the underlying Th2 inflammation for many years before they are graduated to systemic biologics. I think there is a paradigm that needs to change because we're actually putting kids'

lives at risk or we're not carrying as much as we should or do for the best quality of life possible of children and young adults with Th2 inflammation.

So that's where an oral drug with hopefully the safety and the efficacy that we expect should fit in the treatment paradigm to help patients earlier in their trajectory. I'm not saying that this is a patient for mild asthma, a drug for mild asthma, but this is an opportunity to change the treatment landscape in respiratory diseases given that this is a disease of young people, and we need to change how this disease is treated. Maybe, Jared, you can bring us back to where we'll talk more medically.

Jared:

Yeah, no, I think in addition to the important opportunity in pediatric patients, I think also in the adolescent and adult patients with asthma, I think being able to access a much greater proportion of those patients with moderate to severe disease who have a significant unmet need but just are not going on injectable biologics for all the reasons around market access or concerns about being on an injectable or a biologic, to be able to really penetrate the adult and adolescent space as well with our drug for those patients with moderate to severe because now we have an oral drug, which hopefully if it's comparable to dupi in its efficacy and safety, it could really transform how these adult and adolescent patients are also treated with asthma.

Jeet Mukherjee:

Thanks, guys.

Moderator:

Thank you. Your next question comes from Clara Dong with Jefferies. Please unmute and ask your question.

Nello:

I think you're on mute.

Bruce:

Clara, we can't hear you.

Nello:

No.

Bruce

Yeah. Maybe, Operator, do you want to put her back in queue and we go to the next one and she can try to sort that out?

Moderator:

Your next question will come from Alex Thompson. Please bear with us as we invite him to be a panelist. Thank you, Alex, if you'd like to go ahead and ask a question.

Alex Thompson:

Great. Thanks for all the updates here. I guess on the Phase 2b AD study, again, you mentioned obviously patients that had experience with biologics,and I think, Nello, you also mentioned JAK inhibitors. Is there going to be a cap for how many of those advanced therapy experienced patients you might have in the study? And then on rescue therapy, how are you dealing with that as well? Thank you.

Nello:

Yeah, there will be no cap. Again, as long as you have not failed advanced systemic therapies that block this pathway IL4/IL-13, and even JAKs, there will be no cap for those. And I don't think we're discussing rescue therapy. Obviously, there is a system on how we're going to deal with it, but I don't believe we're going to disclose it at this point.

Alex Thompson:

Sounds good. Thank you.

Nello:

Thanks, Alex.

Bruce:

Thanks, Alex.

Moderator:

Thank you. Our next question comes from Faisal Khurshid, Leerink. If you'd like to go ahead and ask your question.

Faisal Khurshid:

Hey guys, thank you for the question. So I know you've put kind of a benchmark out there of 70% to 80% on a TARC reduction from baseline. Could you talk to us about what efficacy

endpoint you think people should focus on given that people are focused on this given that you already showed a nice TARC in healthy volunteers? And then if you're not willing to put out a numerical benchmark, can you just clarify for investors why that's the case.

Nello:

No, so thanks, that's a very good question actually. So we're just basically stating the facts and we've said that this is a biomarker-focused study, mostly because I think we can gather from the data that there is very little, if almost no, let's call it placebo effect on biomarkers. So the absence of placebo should not impact the interpretation of biomarkers. So we're honestly a bit more comfortable saying for TARC, assuming the baseline levels are in the range of what we've seen with the dupilumab study, we expect to see that 70% plus, 70% to 80%. That's a fact, that's what Dupilumab has seen. Now, you would say it's also a fact that the easy reduction on Day 28, there is a number to it.

The reason again, why we've been shy about the putting a number on that is because as you know, clinical endpoints are much more noisy and much more impacted by the potential placebo effect. And so I think we like to be data-driven and a science-first company as you know as well, and I think we will put out things when we can confidently say that those numbers are something that we can scientifically then follow and adhere to. What we said, again, we're not going to hide behind it. The numbers are out there for dupi. I don't have to say what the numbers are. The numbers are out there, the treatment arm numbers are out there. We expect when this study at Day 28 to be in that ballpark because we know that KT-621 blocks the pathway as well as dupilumab. So here is how we've always characterize it and we're not going to change it now a month from the data disclosure.

Faisal Khurshid:

Appreciate it. We'll look forward to the data next month.

Nello:

Thank you.

Moderator:

Thank you. Our next question comes from Judah Frommer, Morgan Stanley, if you'd like to ask your question.

Judah Frommer:

Yeah. Hi, guys. Thanks for taking the question. Maybe just one, if there's anything you can share on early recruitment trends, even anecdotally for BROADEN2. Obviously, the Phase 1b was tougher to recruit just given the 28-days dosing. Here you can get patients on drug for a year plus. And curious about just awareness of the healthies data and how all that might be helping in recruiting patients and what investigator feedback is. Thanks.

Nello:

Yeah. I mean, high level, again, we just started the study. We just activated a few sites, so we're very, very early into that process. I think what we believe right now is even on the Phase 1b, there was a lot of excitement by sites and investigators, and eventually patients we believe, in accessing an oral option. Obviously, the 28-day study was not set up to get patients excited because it's a short study without an OLE. So, the Phase 2b, it's a whole different value proposition and I believe between that, and hopefully the data that we'll disclose in December, I think, we are confident that this will be a study that we can recruit in a timely manner.

Now, recruiting the study as fast as possible is not our goal. Our goal is to recruit the study as fast as possible with the right patient. Going back to what Jared was saying earlier, we have a paranoid oversight of this whole study because we want to try and control the placebo rates as much as possible, even if that has to be at the expense of a week or two or four. So that's where we're coming from, but hopefully we'll be able to share more about your question as we get deeper into the study.

Moderator:

Thank you. We would like to invite Clara Dong to try one more time. If you'd like to unmute yourself and ask your question.

Clara Dong:

Good morning. Can you hear me now?

Nello:

We can hear you. We see somebody else, but we can hear you. Go ahead.

Clara Dong:

Thank you for letting me try again. So, my question is on the Phase 1b trial. So, this trial has a relatively short follow-up four weeks, 20 patients. So, among all the key end points like biomarkers, clinical efficacy, and safety, which ones in your view are relatively less affected by

the treatment duration and which endpoint do you think is more complex to interpret because of the trial design? Thank you.

Nello:

So, I think very quickly, because we're almost running out of time, if you look at the dupilumab study, I don't believe, and hopefully I'm not wrong, Jared, correct me, I don't believe there was any endpoint that reached maximal effect of Week Four. So, I think it's hard for me to say which one is going to be less or more impacted by this 28-day duration. I think we'll look at all the data together in December and answer the question better.

Clara Dong:

Thank you.

Moderator:

Thank you. Our next question comes from Brad Canino, Guggenheim, if you'd like to go ahead and ask your question.

Brad Canino:

Hey, great to see everyone again. Maybe just close out on a capital allocation question for Nello, because you're in the most comfortable cash position you've ever been in with the company, but also have the highest capital demands ever faced by the company. So how do you think about deployment of each incremental investor dollar across KT-621, the named pipeline, and the platform to really maximize value for Kymera at this juncture?

Nello:

Yeah, great question. So I probably need half an hour for this, but in 30 seconds is I think there has never been a biotech company that has developed a program like KT-621 on their own fully. So, we appreciate this is a unique both opportunity and responsibility to do capital allocation the right way. I would also say that if we became a STAT6-only company, we would not be fulfilling the mission that we have of a global company that develops drugs that impact patients across the world with different diseases.

Obviously, there is a happy medium between going all in on KT-621 and spending a lot of money on the other programs. And I always believe that we need to earn the right to invest more. So our ability to invest more in KT-621 will be driven by the success of 621. Our ability to invest more also in other program will depend on also our ability to have success with our clinical

pipeline. So we don't do resource allocation because we have money, we allocate capital because we earn the right to do more. And that's the strategy since day one.

Moderator:

Thank you. Our final question of today comes from Joe Catanzaro, Mizuho, if you'd like to go ahead and ask your question.

Joseph Catanzaro:

Perfect. Thanks so much. Appreciate you guys taking my question here. Maybe a follow-up sort of along the lines of duration of effect, wondering if you could say anything about the level of compliance that you observed in the Phase 1b, but maybe more importantly looking towards the Phase 2b and 16 weeks of dosing, what you guys can do to ensure a high level of compliance there? Thanks.

Nello:

Yeah, no, it's a great question. So obviously with an oral drug, industry data will tell you that getting 100% compliance is difficult just because we all forget to take one pill one day. And with biologics, you can ensure compliance. We're asking patients to be injected in the site. So obviously we're aware of it. We're actually using novel technologies to increase as much as we can adherence to the study protocol with regarding to taking the drug and we're confident that that will deliver what we need.

I will add one last thing, I know we're way out of time, the beauty about a degraded drug is that you can actually skip a dose and maintain maximum pharmacology assuming you have the right dose that reaches complete degradation. That, you will never see with a traditional occupancy-based small molecule inhibitor. So, we have a bit of a cushion on the adherence question, but obviously we're not sitting on it. We need to ensure as much as we can, 100% adherence because we want to maximize the benefit to patients.

Moderator:

Thank you.

Nello:

Great question. Thank you.

Moderator:

I'd now like to turn the call over to Nello Mainolfi for closing remarks.

Nello:

Okay, thank you. I am sorry we ran beyond the 9:30 goal that we had. I want to thank everybody. Obviously, lots of questions. We are always available to continue to engage. This has been the most exciting year of Kymera and we have one and a half more months or so to go. So, stay close, I think it's going to be exciting time in the next few years developing this really once-in-a-generation drug and then the broader pipeline. So, thank you again today and we'll talk more soon.