Kymera Therapeutics First Quarter 2026 Results Call | April 30, 2026

Operator:

Good day everyone. My name is Stefan and I will be your conference operator today. At this time, I would like to welcome you to the Kymera Therapeutics First Quarter 2026 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 Therapeutics' quarterly update conference call.

Joining me today are Nello Mainolfi, our Founder, President and Chief Executive Officer; Jared Gollob, our Chief Medical Officer; and Bruce Jacobs, our Chief Financial Officer.

Following our prepared remarks, we will open the call for questions from our covering analysts. Please use the raise hand icon to indicate you'd like to ask a question, and we kindly ask that you limit your question to one so we can accommodate everyone.

But before we begin, I'd like to remind you that today's discussion will include forward-looking statements subject to risks and uncertainties described in our most recent Form 10-Q filed with the SEC. Please note any forward-looking statements speak only as of today's date and we undertake no obligation to update them.

With that, I'll now turn the call over to Nello.

Nello Mainolfi:

Thanks, Justine and thanks everyone for joining us this morning.

Next week marks the 10-year anniversary of Kymera's founding, and it represents more than just a milestone. We have stepped into a new chapter, where we believe the strong foundation we've built over the past decade positions us to deliver transformative medicines for patients around the world.

In the past 10 years, we have built unique capabilities including: Our hit finding approach to identify ligands to historically undrugged proteins. Building on that, creating new rules on how we identify drug-

like highly specific and potent degraders. Importantly, key insights to deliver high fidelity of clinical translation. And finally, creative early clinical studies to de-risk clinical development, late clinical development.

We have continued to refine our target selection strategy such that we believe we have built one of the most compelling oral, small molecule pipelines in the industry.

As we look to the next decade, our guiding principles remain unchanged. We'll continue to focus on bold science, demonstrate early proof-of-concept to support our investments, and build medicines that we believe can change the standard of care for many diseases. And, we'll obviously be looking to make the final step, becoming a fully integrated global commercial company that delivers groundbreaking medicines for patients around the world.

And it's these principles that have shaped our innovative and increasingly differentiated pipeline.

We are laser-focused on our wholly owned programs, such as KT-621 and KT-579, where we're applying targeted protein degradation to well-validated, disease-relevant pathways in immunology. At the same time, we're extending our reach through partnerships, like our work with Gilead advancing KT-200, our first molecular glue program and Sanofi with IRAK4.

What ties it all together is our commitment to pursuing high-value, disease-driving targets with precision, and to do it repeatedly across different therapeutic areas. That sharp focus, and the consistency of results we have delivered, is what gives us confidence not just in individual programs, but in our ability to broaden and expand our pipeline.

We've done a lot of the groundwork over the past few years, as we sit here today, we're well positioned to execute on our strategy and deliver on the groundbreaking promises of our programs.

Our immediate priority is execution of the two KT-621 Phase 2b studies.

In atopic dermatitis, we're on track to complete enrollment this year in the BROADEN2 study, and we expect data by mid-2027. We continue to be encouraged by the level of interest from both investigators and patients, and it's clear the enthusiasm for the trial is high. We are tracking with our internal expectations for asthma as well, where the BREADTH study readout is expected by the end of 2027.

As we advance these studies, we'll continue to assess a broader development strategy, including areas such as COPD, EoE, Chronic Rhinosinusitis and others, to maximize the value of the program.

Turning to IRF5, we expect to report healthy volunteer data from the KT-579 Phase 1 study in the second half of 2026. The overall goal is to demonstrate that we can safely degrade the target, and the biology translates in humans in a way that's consistent with what we've seen preclinically.

IRF5 has been a target of particular interest across the industry for a very long time. Jared will spend more time on this opportunity, but what's compelling here is that by selectively degrading IRF5, we have the potential to impact multiple key drivers of disease with a single mechanism. If we think about lupus specifically, we're addressing autoantibodies, type 1 interferon, and pro-inflammatory cytokines, all through one pathway. While individual drugs can address each specific pathway, we believe a single

mechanism such as an IRF5 degrader has the potential to address all pathways and potentially have greater therapeutic potential.

We also have several opportunities emerging in our early research pipeline and expect to disclose the next target later this year when we reach development candidate.

Before I move on, I wanted to touch briefly on our Gilead collaboration. We recently announced that Gilead has made the decision to advance KT-200, our CDK2 molecular glue, which could enter the clinic as early as next year.

This program is a great example of the power of Kymera's R&D capabilities. Our ability to reach a target like CDK2 with a highly selective molecular glue really speaks to the depth and reach of our capabilities.

CCNE amplified tumors need specific agents to address the underlying biology. CDK2 selective blockade has not been achieved by any investigational drugs, in my opinion, mostly because of the homology and cross reactivity with CDK1. We designed an absolutely selective molecular glue degrader to achieve this target product profile. I'm thankful to Gilead for believing in this program early on and now for taking KT-200, Kymera Therapeutics discovered development candidate, into development. Special thanks to our CDK2 team for delivering this molecule in record time.

So, everything we're doing across all these programs is to build long-term value. This isn't just about incremental progress. It's about our commitment to developing medicines that we believe can change treatment paradigms and expand access to important treatment options.

KT-621 is the best example of our strategy in action. Our continued engagement with KOLs reinforces the growing anticipation for a therapeutic that can potentially fundamentally change the treatment paradigm in Type 2 inflammatory diseases.

As you all know, we have shared compelling data sets, including most recently at AAD. With that as a backdrop, I thought it was worth stepping back and framing what makes this opportunity so compelling.

When it comes to treating these conditions, patients and physicians are often forced to make tradeoffs. What they want most is simple: a safe, effective and convenient option. We believe KT-621 is well positioned to meet that need, with the potential to deliver the efficacy of biologics and the convenience of an oral pill.

And that matters, because patient preference is clear. Given the option, many would choose oral therapy over the burden of injections, especially for chronic diseases that require long-term treatments.

In fact, most patients are being treated with suboptimal therapies, such as topical creams, which can be messy and ineffective, or with inhaled medicines, often because they or their prescribers are not comfortable moving to advanced systemic injectable therapies.

KT-621 can change this dynamic completely. Allow patients that are not well treated by these local therapies to access a simple, accessible, effective and trusted oral pill.

So, when you put all of that together, the mechanism, the clinical profile, and the simplicity of administration, we believe KT-621 can stand on its own and has the potential to represent a true paradigm shift. As a result, our focus is to expand the market and redefine what patients and physicians should expect from treatment.

When you take a broader view, the scale of the opportunity really comes into focus. This is a slide you've seen before, but it's worth revisiting because it highlights just how much untapped potential still exists in Type 2 inflammatory diseases, particularly for new entrants that can expand the market.

Importantly, nearly 50 million patients could benefit from better therapies. This opportunity is not just about taking share from existing treatment, it's about reaching the much larger population of patients who are untreated or under-treated today.

We're already doing the work to better understand the patient population, market dynamics, and access landscape, and these insights are guiding our development and, ultimately, our commercial strategy.

If successful, KT-621 could become the preferred option and potentially shift treatment earlier in the disease course, where earlier intervention could meaningfully reduce disease burden and progression.

At AAD and through recent advisory board meetings, the feedback has been consistent. There is clear demand for a convenient, effective oral option and strong excitement around this mechanism.

With that, I'll turn it over to Jared to discuss our clinical pipeline a bit more, including KT-579. Jared?

Jared Gollob:

Thanks, Nello. Given the growing focus and attention on our IRF5 program, I'd like to use most of my time this morning to highlight why we are enthusiastic about this program and target.

There is a significant unmet need in autoimmune diseases like lupus, which are characterized by broad immune dysregulation rather than disruption of a single pathway. While biologics have successfully validated individual targets, such as Type I interferon, proinflammatory cytokines, and B cells, these approaches act downstream and only narrowly address the underlying disease biology. As a result, many patients continue to experience inadequate responses.

This is where IRF5 becomes particularly compelling. It is a genetically and biologically validated transcription factor that functions as a master regulator and central amplifier of immune responses across multiple autoimmune diseases. When dysregulated, it drives coordinated activation of multiple inflammatory pathways, effectively locking the immune system into a persistent inflammatory state. Importantly, human genetic data connect increased IRF5 activity to these pathways that are known drivers of autoimmune disease.

This biology supports our confidence that modulating IRF5 has the potential to translate into meaningful clinical benefit.

KT-579 is designed to selectively degrade IRF5 and thereby rebalance immune activity by simultaneously modulating multiple downstream disease-driving pathways. Our goal is to rebalance the immune system

more comprehensively and deliver a durable response compared to injectable biologics that target single pathways, while also offering the convenience of oral dosing.

We continue to generate compelling preclinical data demonstrating activity across multiple disease-relevant models. These results reinforce our confidence in IRF5 and support the potential for KT-579 to offer clinical benefit. We plan to present preclinical data, including new data in IBD models, at DDW next month and FOCIS and EULAR in June.

We have already generated a robust preclinical data package and have shown that we can effectively and selectively modulate this central node of inflammation.

As you'll see here in our lupus models, KT-579 demonstrated strong and durable activity, associated with deep IRF5 degradation.

Importantly, the level of activity observed compares favorably to both approved therapies and other clinically active agents evaluated in similar preclinical settings.

Taken together, these data further support the potential of IRF5 degradation to drive meaningful disease modification in autoimmune conditions like lupus and IBD.

I should also note that from a safety perspective, IRF5 is not essential for host defense against infectious pathogens, which suggests there may be an opportunity to modulate the immune system through IRF5 targeting without the risk of bacterial or viral infections. IRF5 knockout mice do not show any susceptibility to infections, and in our 4-week GLP tox studies in non-human primates and rodents we did not observe any adverse findings.

We've now advanced KT-579 into the clinic.

The Phase 1 healthy volunteer study is designed to evaluate single- and multiple-ascending oral doses, with a focus on achieving >90% IRF5 degradation in blood and a favorable safety profile.

We will also assess pharmacodynamic activity using ex vivo stimulation assays to understand the impact of IRF5 degradation on key inflammatory pathway biomarkers upregulated by TLR7, 8 and 9 agonists, including Type 1 interferons, proinflammatory cytokines and inflammatory pathway gene transcripts. It's our expectation that we should see a 50-80% reduction in these biomarkers across the three TLR pathways assessed if we're engaging IRF5 effectively, which would suggest the potential for IRF5 degradation translating into clinical activity in subsequent patient studies with KT-579.

Looking ahead, we expect to report Phase 1 healthy volunteer data in the second half of 2026. Following that, we are planning a proof-of-concept study, likely in lupus, where genetic and biological rationale for IRF5 targeting is particularly strong. We will share more details on the planned design later this year.

Before I wrap up, I did want to touch briefly on our STAT6 program.

There continues to be a lot of excitement around new mechanisms in AD and KT-621's profile continues to resonate well.

Last month we had the privilege of presenting the KT-621 Phase 1b BroADen data at AAD during a highly attended late breaking trial results session.

In addition to the presentation, we had a strong presence at our booth at AAD and meaningful engagement with the AD patient community, including patient support groups, which reinforced the real need for new treatment options and excitement over the potential of KT-621 to provide an effective and safe oral therapy for AD. We also connected with a number of KOLs and investigators, who shared their enthusiasm for KT-621 and viewed it as one of the most promising new approaches to treating AD.

New in the AAD presentation was the first detailed look at impact on body surface area, or BSA, a measure of the extent of AD skin lesions. We saw an overall mean reduction in BSA of 49% at 4 weeks across the two dose groups reflecting a substantial reduction in disease burden. This, like other key clinical efficacy endpoints, including EASI and pruritis, was in line with published data for dupilumab at Week 4.

These early data continue to highlight the potential of KT-621 in AD, and we look forward to learning more in our randomized, placebo-controlled Phase 2 studies. We are actively enrolling the KT-621 Phase 2b BROADEN2 and BREADTH studies in AD and asthma and look forward to sharing data from these studies by mid-2027 and late 2027, respectively.

Overall, we are highly encouraged by all the progress with both KT-621 and KT-579 and look forward to keeping you updated as these program progress in the clinic. With that, I'll pause here and turn the call over to Bruce.

Bruce Jacobs:

Thanks, Jared.

As I walk through the first quarter results, please refer to the tables found in today's press release, which was filed this morning.

Collaboration revenue in the first quarter of 2026 of $34.4 million is attributable fully to our Gilead partnership.

More broadly with respect to Gilead, we received an upfront payment of $40 million upon signing the licensing and option agreement last year, which now has been fully recognized in our revenue. As Gilead has exercised its option on KT-200, we are due to receive a $45 million investment from Gilead which is expected to be recognized as revenue in the second quarter of 2026. And as a reminder, under this agreement, we are eligible for approximately an additional $700 million in total milestone payments.

Also on the partnering front, we continue to expect Sanofi to advance KT-485 into Phase 1 testing this year, which will include the receipt of a milestone upon dosing the first healthy volunteer. As a reminder, under the structure of the Sanofi agreement, we have the potential to realize nearly $1 billion in total milestones.

Now, with respect to operating expenses, R&D for the quarter was $98.2 million. Of that, approximately $8.6 million represented noncash stock-based comp. The adjusted cash R&D spend of $89.6 million,

which excludes that stock-based comp, reflects an 18% increase from the comparable amount in the fourth quarter of 2025.

On the G&A side, our spending for the quarter was $20.4 million dollars, of which $7.4 million was noncash stock-based comp. And the adjusted cash G&A spend of $13.0 million, again, excluding that stock-based comp, reflects a 30% increase from the comparable amount in the fourth quarter of 2025. I should note that this quarter's G&A growth was elevated relative to our typical run rate, primarily driven by the timing of certain expenses. With that said, we expect G&A growth to moderate in the coming quarters.

And finally, we ended March with a cash balance of $1.55 billion, providing runway into 2029. This allows us to complete both the KT-621 Phase 2b trials in AD and asthma, and to fund a large part of the first Phase 3 trial for KT-621 in AD. The runway also allows us to advance KT-579 through initial proof of concept testing, to progress our research pipeline and to grow our organization and build our capabilities as we prepare for later stage development and, ultimately, commercialization.

Overall, we remain well positioned, and well capitalized, to execute on our clinical programs and pipeline.

With that, we'll pause while we regroup in our conference room and assemble the queue for your questions. Thank you.

Stefan:

Thank you. At this time, if you would like to ask a question, please click on the raised hand button, which can be found on the black bar at the bottom of your screen. If you've joined by phone, please dial star nine on your keypad to raise your hand. When it's your turn, you'll receive a message on your screen inviting you to join as a panelist. Please accept and wait until you're promoted to panelist. Please unmute your audio, turn on your camera, and ask your question. As a reminder, we are allowing analyst only one question today in order to accommodate everyone. We'll now pause a moment to assemble the queue. Our first question will come from Ellie Merle with Barclays. Please unmute your line and ask your question.

Jasmine Fels:

Hi, this is Jasmine on for Ellie. Thank you so much for taking our question. I just wanted to ask a bit more about the IRF5 data in healthies we expect later this year. So, in your remarks, I know you said you're looking for 50 to 80% modulation of the biomarker pathways in the ex vivo stimulation assays. Can you help us understand a little bit better how you get to that threshold and elaborate on what you would expect this to translate to clinically?

Nello Mainolfi:

Yeah, thank you. Maybe I'll start and then pass it to Jared to spend a bit more time on the details. So obviously whenever we set out these, expectations are always based, especially for the first human

translation or our preclinical data, just remember this is a critical node that actually intersects three key pathways. So we see that when we block this node, we don't need to even get above 90% degradation. We're able to see modulation of a series of downstream biomarkers. Maybe Jared, you can speak to how we come up with those numbers.

Jared Gollob:

Yeah. So we assess these pathways, in particular the TLR7/8/9 pathways with ex vivo stimulation of whole blood. That's how we're planning to do it in the Phase 1 using agonists to the TLR7, 8, and 9 receptors. So essentially, the way we came up with 50 to 80% is that our expectation based on our preclinical in vitro data is that if we're able to degrade IRF5 by at least 90%, we should be able to see that range of blockade of these particular pathways. Now that 50 to 80% is approximate. Whether we end up seeing within that range or more than that remains to be seen, but that's an approximate level that we would expect to see of inhibition in conjunction with at least 90% degradation of the target.

Nello Mainolfi:

And maybe just to add, if this was a single pathway like we've seen, for example, ‘621 with STAT6, and we have a downstream biomarker that is activated, obviously we expect complete blockade of that one biomarker, but given that these are multiple pathways and these pathways also signal to other receptor, this is why there is a range because it depends on what pathway, what stimuli, what biomarkers. That's why there is a bit more nuance into this biology.

Jasmine:

Okay, that's helpful. Thank you. And then one quick follow-up. Should we expect enrollment completion for the ‘621 AD study as more of a near-term event or likely later in the year based on the trends that you're seeing?

Nello Mainolfi:

Yeah, great question. Look, I think we've said it from the beginning of the study, we expect to complete enrollment by the end of the year, so we're going to stick with that guidance. I think the expectation will be that when we complete enrollment, we will communicate it.

Jasmine:

Okay, thank you.

Stefan:

Our next question will come from Brian Cheng with JPMorgan. Please unmute yourself and go ahead.

Brian Cheng:

Hey guys, thanks for taking out questions this morning. It's great that you have laid out the expectations for IRF5 degradations in healthy volunteers, but just kind of looking ahead into lupus patients, do you have a sense of the level of IRF5 degradations that we need to see in lupus patients where you start to see some clinical benefits? And in other words, is there a minimum threshold of IRF5 degradation that you need to hit in patients? And for this mechanism, how translatable is it from healthy volunteers to patients in terms of IRF5 degradations? Thanks for taking our questions.

Nello Mainolfi:

Yeah, no, thanks, Brian. So, let's start with what we're trying to do here. So, as we've done now, this is the sixth program. The human translation is focused on understanding key parameters, which is, what is the exposure in dose needed to achieve a level of degradation X, and then what level of degradation X translates in terms of clinical benefit as well as safety in patients. So, we always do this in multiple steps, as you know. So right now, what we're trying to figure out is, what is the dosing exposure that gives us the level of degradation that we believe is therapeutically relevant? Based on preclinical data, and as you know well, if the preclinical animal model data would always translate in humans, we would've cured all diseases. So, all these preclinical data have to be taken with a grain of salt. But what we've learned preclinically is that as low as, let's say, 80% degradation is sufficient to drive, let's say, efficacy benefit in this mouse model, benefits that actually are comparable in many cases superior to standard of care or drugs in development.

So, with that in mind, our goal is always to being able to demonstrate more than 90% degradation, because that gives us the flexibility to then titrate back in a dose ranging study and establish, as we're doing for ‘621 now, what is the level of degradation needed to achieve maximal and minimal efficacy. So that's the same we're going to do with ‘579. I think we want to establish, as Jared said, robust degradation, we want to see more than 90%, knowing that that might not be necessary, but for us, I think it's important to demonstrate that. And then translation of degradation between healthy and patients, which was the second part of your question, historically, we have never seen a difference of degradation between healthy volunteers and patients. Remember, these are catalytic molecules that do not perform depending on expression of targets, but actually perform depending on exposure of drug and thresholds of exposure. So, we expect that whatever we see in healthy volunteers will translate in patients. We've shown that with ‘621, we've shown it with IRAK4, we've shown it also in other programs in other disease areas.

Brian Cheng:

Great. Well, thanks Nello.

Nello Mainolfi:

Thank you. Thanks, Brian.

Stefan:

Our next question will come from Faisal Khurshid with Jefferies. Please unmute your line and go ahead.

Inanc Caner:

Hi guys, this is Inanc for Faisal. Just wanted to ask about the initial enrollment in BROADEN2. Have the initial patients tracked with your expectations with respect to the baseline characteristics? And thanks so much for taking our question.

Nello Mainolfi:

Thank you. Great question. So, I think we're not going to comment on where we are with baseline characteristics. I think it's a bit of a futile exercise until we complete the study and share the data. What I will say, historically, we've said that if you look at the early dupilumab studies, the baseline entry criteria in terms of severity of disease, you have been historically higher, meaning more severe than more recent studies. And that have been...we said also historically that there are maybe two main reasons. One is that given that there are drugs on the market, more severe patients, especially in these highly advanced, sophisticated clinical centers, so more severe patients have access to these therapies. And also, generally, the other main reason is to be because of the competitive landscape and the general, again, the way that sites and investigators enroll in these studies, you've seen a bit more of a less severe population in studies.

And I'm not talking about our studies, I'm talking about studies in the past, I would say five to six years. So we continue to have this expectation that a study that is run today, a global study, has a mean baseline that is in the mid-20s based on what we've seen historically, what we've seen in the 1b, but I'm not going to comment about what we're seeing in the current study. We'll do so when we release the data.

Inanc Caner:

Great. Thank you so much, guys.

Stefan:

Our next question will come from Brad Canino from Guggenheim. Please unmute your line and ask your question. Okay. Whilst Brad is just asking his question, we'll just move on to Biren Amin with Piper Sandler. Please unmute your line, turn on your camera and ask your question.

Biren Amin:

Yeah. Hi, guys. Can you hear me?

Nello Mainolfi:

Biren, try again.

Biren Amin:

Can you hear me now?

Nello Mainolfi:

Not great.

Biren Amin:

Okay. Maybe just to start [inaudible]...

Nello Mainolfi:

Biren, it's not working. Maybe you can try again in a bit, or I don't know if you're underground. Give it a shot in a couple of minutes. We'll circle back.

Stefan:

Thank you, Biren. We'll move on to Brad Canino with Guggenheim. If you could unmute your line and ask your question. Thank you.

Brad Canino:

Hey, great. Good to see everyone. Good developments with Gilead and the molecular glue for the CDK2. I'm wondering if you could just discuss what technology advances the Kymera scientists have been able to unlock for this technology and how to achieve the needed protein-protein interactions. And should we expect more named pipeline molecules to emerge as glues over the next few years? Thanks.

Nello Mainolfi:

Yes, thanks, Brad. And I think you know Kymera well enough to know that we've always looked at the technology as a mean to unlock value for patients through going after difficult to drug or undrugged targets. And so we always look at what is the right technology for the right target. So CDK2 is a very interesting problem.

We know that if you have CCNE amplified tumors, there is a mechanism of resistance to 4/6 that goes through CDK2. Now, if you can get to CDK2 either alone or probably more excitingly in combination, you can really have profound effect in breast cancer and other type of solid tumors that unfortunately affect lots of women. And so what has been the challenge with CDK2 has been that there is a high structural homology between CDK2 and CDK1, and CDK1 doesn't actually bring any benefit to efficacy and actually only brings safety issues.

And the comment I made earlier, which I'm really comfortable standing by, I don't believe there are absolutely selective CDK2 agents out there, at least in our hands. And so you're going to run into dose limiting toxicity. I'm sorry if I'm going too long here. We're going to run into dose limiting toxicity

because CDK1 comes in play and you actually do not exploit fully the power of CDK2 either mono or in combination.

So why we using molecular glues for this target is because in the traditional binding site that people use for CDK2, which is the ATP binding pocket, there is just high structural homology. We have published on an ATP binding site-based heterobifunctional degrader and while we were able to have enough selectivity, it wasn't good enough for us. So, we moved on from that effort. And so, we said, how do we get absolute CDK1 selectivity? We did it through a protein-protein interaction enabled molecular glue that is outside of the ATP binding pocket.

So, this is the premise to my answer, which is yes, you should expect Kymera to have other programs from our pipeline that will use this concept because this is just a continuation of protein degradation. It's just, again, solving a different problem with a slightly different solution. And yes, we expect to see more from there in any therapeutic areas. This is not just relegated, let's say, to oncology.

Stefan:

Thanks. Our next question will come from Geoff Meacham with Citi. Please unmute your camera and your audio and ask your question.

Nishant Gandhi:

Hey guys, this is Nishant on for Geoff. Thanks for taking the question. I want to go back to the data you presented at AAD. So, in terms of the body surface area, you saw higher reduction at 100 milligram versus 200 milligram, so you didn't see much dose response. Is this simply a small sample noise or is there a pharmacological explanation such as maximal degradation plateau effects?

Nello Mainolfi:

Yeah, actually I'll let Jared to actually speak to the data. I just want to remind you and everybody that 100 milligrams and 200 milligrams gave the same degradation, hence we expect to see similar activity. But Jared, maybe you can speak to BSA, which I actually don't remember.

Jared Gollob:

Yeah, if you look at the error bars on those graphs, they're actually overlapping. And so differences between 100 and 200 milligrams are really not significant differences, and it's probably a function of the small ends. I think whether you look at BSA or EASI or the other clinical endpoints that we looked at three or four weeks in that study, you don't always see complete overlap of the curves, but you do see overlap of the error bars. So, I think that tells us that we're seeing comparable activity across both doses, across multiple different endpoints.

Nishant Gandhi:

Got it. And just to follow up on that. In terms of EASI versus BSA, you see a gap in magnitude, again, given it's a small sample size. Is this expected given that EASI captures both extent and severity while BSA measures just extent alone? Does this suggest to you that there is deeper severity improvement with this molecule versus surface area clearance at four weeks?

Nello Mainolfi:

Can I just jump into this, Jared?

Jared Gollob:

Mm-hmm.

Nello Mainolfi:

I'm not going to actually address a specific question. I just want to say that I've said multiple times, let's try not to over-interpret the individual numbers in such a small study with, as Jared said, the confidence interval between the two doses were almost completely overlapping. I think the important take home from the study is that all these measures show the robust effect consistent across all measures and consistent with upstream biologics. But Jared, if you want to add on the particular topic.

Jared Gollob:

No, I think your point is a main one. I think BSA and EASI, there are overlapping, but distinct measures. As you said, BSA is looking more at the extent of disease. EASI is taking into account both the severity of individual lesions as well as the extent of disease. So, there's an overlap there, but the bottom line is that we're seeing a comparable robust effect on both of those endpoints with KT-621.

Nishant Gandhi:

All right. Thank you.

Stefan:

Our next question will come from Mayank Mamtani from B. Riley Securities. Please unmute your line and ask your question.

Mayank Mamtani:

Yes. Good morning, team. Thanks for taking our questions, and congrats on the progress. So on STAT6, there's a lot of activity in the inhibitor landscape, for example. So, I was just curious what questions, Nello, you have for some of these highly potent claim to be selective approaches emerging. From the preclinical data, KT-621 does stand out based on whatever's available, but we'll probably get some clinical data next year from you and others. So just curious, how do you expect the clinical data here to maintain your leadership? And then just quickly on the ‘621 physician excitement maybe between AD

and asthma, and recognize you are yet to present your data at ATS next month. Any thoughts between the two indications, the importance of oral versus maybe less frequent injectable, if you've teased out what matters more to the different set of clinicians?

Nello Mainolfi:

Okay. Well, those are two robust questions. So, on the first one, thank you. So, on the first one, small molecule degraders, we've touched on this also extensively in the past. So first of all, recognize that STAT6 has been seen as a key difficult undrugged target, but huge potential for more than a decade. So it's actually quite exciting to see so many companies, large and small, pouring hundreds of millions of dollars into this mechanism. Mostly I would say following the exciting data that we started to share as early as January of '24, but obviously we've been working on these targets for multiple years. So, I think it's great, first of all, that there is a lot of enthusiasm around this target.

The reason why we believe that degraders are going to be highly differentiated is because we are so fortunate that while obviously technology requires a level of understanding that is not easily commoditized yet. So, these molecules though, with obviously the challenge that it takes to make highly specific and potent degraders, the upside is that today are catalytic in nature and require exceptionally low exposures. We're talking about nanomolar to picomolar to completely remove STAT6, which allows us to have complete degradation at very low doses and importantly at very low exposures so that we can deliver a drug once a day. And actually technically you could probably deliver a drug less frequently than once a day.

With a small molecule inhibitor, as you know, you're inhibiting stoichiometric in the target. So, one molecule blocks one protein. So for this type of protein, you require a large amount of molecules in the body, in all tissues, for 24 hours. And this becomes a challenge with regards to PK exposure, safety and therapeutic index. And so in our experience, and I think we've said this publicly, we've invested actually quite heavily in small molecule inhibitors to actually answer the question, do we need a degrader if an inhibitor is good enough? Our answer is yes, you need a degrader because inhibitor can't quite reach the level of pathway blockade that a cytolytic degrader can.

So, I think the beautiful thing about drug development is at the end of the day, I can spend the next hour trying to convince you that I'm right, but the best thing is that we'll generate data soon enough. And I think that will be the final nail on the coffin on this argument for us, I hope.

With regards to your second question. So, we've had the fortune, and hopefully we did also something good, about generating and importantly presenting our data in many medical conferences. We were fortunate to be selected at the podium at EADV, which I believe was probably the first time for healthy volunteer data. I might not be sure. And then we presented AAD. We presented ATS last year, preclinical data we'll present later. So, there is a very high appreciation from the medical community, both AD and asthma, about the potential of an oral drug in the space. I just want to remind you whether it's AD or asthma, the majority of patients are not controlled well or not treated well with either local therapy like inhalers or topicals, and not enough of them are on advanced systemic biologics.

So, our goal is not to compete with less frequent dosing. That might come in place just the market dynamics, but we're actually trying to mobilize the millions of patients that are sitting on the sidelines because they feel or their prescribers feel they're not ready for an injectable biologics and we offer that biologics like oral pill that will change their lives.

And so I think we're seeing in other disease area, it's a complete different paradigm shift, and that's really what we're focused on. I think this obviously resonates with investigators and more importantly, resonates with patients based on our experience.

Mayank Mamtani:

Thank you, Nello.

Nello Mainolfi:

Thank you.

Stefan:

Thank you. Just as a reminder, if we could just stick with one question just to accommodate everyone today. Our next question will come from Judah Frommer with Morgan Stanley. Please unmute your line and go ahead.

Judah Frommer:

Yeah. Hey guys, thanks for taking the question. Maybe just building on the last one, I think it's fair to say you've established a playbook for Phase 1 studies in AD. So just curious to get your take on that excitement for ‘621 on the oral aspect versus the mechanism aspect. There are others going after oral drugs, but maybe a more novel target. So the level of excitement for the oral nature of the drug, but also the fact that you're hitting IL-4/13, which is so well understood by docs. And then just within the landscape, curious specifically maybe on anything around IL-18 that you see as interesting within AD or more broadly and how that could apply to the IRAK4 program. Thanks.

Nello Mainolfi:

Yeah. Thanks, Judah. I like your 90 years in your backdrop. You're 80 years older than Kymera at Morgan Stanley. So yes, to answer your question, I think you put it exactly right. The reason for the excitement for ‘621 is not just about the oral drug. I think it's the combination of oral, which is needed in these still early markets, but combine it with the sense of understanding and comfort of well-validated pathways like IL-4 and 13. And I think that's really what's making this drug and this program very unique in the space.

As you know, well, there are several other potential oral mechanisms out there, which to be honest, I hope that they have a path forward beyond early Phase 1 data. I think obviously what the burden of proof for a mechanism in the IL-4 and 13 pathway, I assume is a bit less than it is for completely new

pathways with completely unproven efficacy and safety. So, I don't know, Jared, if there was anything to add to the second part.

Jared Gollob:

Yeah. And the only thing I would add to the first part too is just around, because you talked about mechanism, Judah, and I think there is an appreciation that the unique TPD mechanism, that catalytic mechanism of action that can lead to durable, maintain, complete target suppression of pathway suppression that equals what you can get with upstream injectable biologics. I think that's a big selling point here with regard to degraders versus small molecule inhibitors.

You asked about IL-18. IL-18, some of those initial data coming out of Evommune are interesting, and I think it speaks to the fact that AD does not have just one flavor of inflammation. Obviously, Th2 is one of the main drivers of the pathophysiology, but other types of inflammation, whether it be Th1, Th17 driven, probably have some contribution as well. And seeing activity with a drug targeting IL-18 probably speaks to that.

Again, it's not as well validated a pathway here in AD. It's interesting to see the results coming out of that. And it makes one think of interesting possibilities down the road maybe for combination therapies by bringing on other drugs that are hitting other types of inflammation in addition to Type 2 inflammation.

Judah Frommer:

Thanks.

Stefan:

Our next question will come from Biren Amin with Piper Sandler. Please unmute your line and ask your question.

Biren Amin:

Yeah. Hi, guys. Can you hear me?

Nello Mainolfi:

Yes. Yeah, yeah.

Bruce Jacobs:

Yes.

Nello Mainolfi:

All right. So on BROADEN2, I noticed in the press release that you're also including adolescents in addition to adults in the trial, but I think more recently there was some inclusion criteria changes in the trial where you're now requiring, I think, adult patients needing at least three years of chronic disease, whereas with adolescent, it's a requirement of at least one year. Can you just maybe talk about the implications of that change?

Nello Mainolfi:

Yeah, so the addition is the inclusion of adolescents to the study. Again, this is part of our overall strategy to change treatment paradigm for adult. And more importantly, I would say for young children and adolescence is step one. This is a disease of young children usually diagnosed in your first probably six years of life, and a drug like ‘621 could have a huge potential in children. So that's the main reason why we want to study this drug in younger population as early as possible.

Jared, I don't know if you want to comment to the inclusion-exclusion criteria.

Jared Gollob:

Yeah, I think in terms of inclusion-exclusion, when you categorize your criteria for AD, you want to make sure that your patients have AD. So, one element of that to make sure you're getting patients with that diagnosis is they need to have a diagnosis for a certain number of years. So, for adults, obviously because they're older, the cutoff there is at least three years. With adolescents, because they're younger, had the disease for a shorter period of time, there's a one-year cutoff. And again, the reason for both of those is to give you increased certainty that these patients truly have a diagnosis of AD.

Biren Amin:

Got it. And then maybe just one question on IRF. There's clearly IRF translocation in naive B cells, plasmablasts, and monocytes in patients with lupus. I know translocation, healthy volunteers is low, but is there anything you could do ex vivo to evaluate the impact of IRF degradation on translocation?

Nello Mainolfi:

Yeah, it's unlikely that we're going to see activation or translocation IRF5 in healthy volunteers. So I don't think that's what we're going to be looking for. We're going to be, as Jared said, looking at ex vivo stimulation of the blood, with or without translocation. Again, I think it's probably close to 0% chance we'll find that in healthy volunteers, but we'll interrogate pathway regardless of that. All right, next one.

Stefan:

Our next question will come from Alex Thompson with Stifel. Please unmute your line and go ahead.

Alex Thompson:

Great. Good morning and thanks for taking our question. Maybe again on the ongoing AD and asthma studies, could you talk a little about more color on enrollment progress, site activation, your level of oversight of these sites? And then maybe could you tell us how many patients have been dosed at this point across both studies? That'd be helpful. Thanks.

Nello Mainolfi:

Yeah, no, obviously great question. As I said, we're trying not to comment on these things. Not because we want to be secretive, I think it's only productive to do it at the end. I think what I can say is that the studies are on track in both in terms of site activations and patient enrollment. And so the timelines that we put out are obviously still relevant. As I said, I think the best way to manage this particular question is as soon as we complete enrollment, we will communicate and then maybe then we can answer more specific questions about what we've seen and pace of enrollment, activation, et cetera.

Alex Thompson:

All right. Thanks.

Stefan:

Our next question will come from Marc Frahm with TD Cowen. Please unmute your line and ask your question. Marc, please unmute your line and ask your question.

Marc Frahm:

Great. Thanks for taking my questions. Maybe just back to prior comments about the attractiveness of oral options and the enthusiasm also for the mechanism. I mean, can you contrast ‘621 with the IL-23 space because we're seeing that launch just starting now in the psoriasis space. And just how much should we view the success hopefully of that product as a proxy for ‘621 versus how different do you think these markets are in terms of their eagerness for an oral therapy?

Nello Mainolfi:

Yeah, thanks, Marc. I don't want to hitch your wagon onto any other mechanism or drugs because we don't control those. But it is a fair point that I think we're seeing finally something we've been saying for a while, which is a novel oral mechanisms that can deliver in some cases close to biologics-like activity having a ton of enthusiasm. Obviously, the psoriasis market is very mature. There are drugs that you can dose every three months, or even less in some cases, that are extremely effective. We're seeing even less frequent dosing. Obviously, you start to wonder what's the driver for that, but that's likely it's not what we're working on.

And so the question is very much your market, can an oral drug with good efficacy and safety even impact the landscape? And it looks like it will. I mean, I was at AAD and lots of, not to advertise for J&J, our friends at J&J, but lots of dermatologists were super excited about that drug. So clearly, even in a

well-established, super mature market where there are already multiple blockbuster drugs, a drug like that seems to be highly differentiated.

So, we're talking in AD where there is no oral drug with good safety and efficacy. There is really only two category of drugs approved, an IL-4, 13, and then all the other IL-13s that are not differentiated, and JAK inhibitors. So this is where psoriasis was 10 years ago. So, bringing to the market something that is so differentiated so early in the treatment, in the market evolution I think will have a much bigger effect than what we might be seeing with IL-23 in psoriasis. So, I think it validates, but more importantly, I think our opportunity is probably much more impactful given, again, the maturity of that market.

One could point to the obesity space, but that's a whole different market dynamics. But you're seeing also there, these new orals are activating mostly new patients, right? And that's really, I think what many of these oral drugs are there to do, is to really serve the millions of patients that are not on these advanced therapies.

Stefan:

Thank you. Our next question will come from Joseph Catanzaro with Mizuho. Please unmute your line and go ahead.

Joseph Catanzaro:

Hey, great. Thanks, guys, appreciate you taking the questions. Quick one from me along the lines of ‘579's preclinical data at DDW, and maybe also your comments on mechanism earlier, but there seems to be a growing effort towards developing combination therapies in IBD. So wanted to ask about IRF5's mechanism and where you see it as most orthogonal or complementary with existing mechanisms in IBD like alpha4beta7, IL-23, TL1A. Thanks.

Nello Mainolfi:

Yeah, fortunately ... I'll let Jared answer this one. So, Jared, I’ll give you 30 seconds to come up with an answer while I say what I'm going to say. So fortunately, I think what we're trying to do here at Kymera is bringing a completely new mechanism to the IBD space, hopefully. Obviously, we haven't committed to developing in this space yet, but versus obviously combining existing mechanism or other things. But, Jared, maybe you can speak to the science.

Jared Gollob:

Yeah, I mean, I think one of the great aspects of IRF5 is that it really controls circling through multiple different pathways. We talked about type-I interferon, we talked about B-cells and autoantibodies, but also myeloid cells, monocytes, potentially neutrophils, also dendritic cells. And when it comes to inflammatory bowel disease, the myeloid component in particular is very important in diseases like ulcerative colitis. For example, we have cytokines like IL-12, TNF, IL-6, and others that are driving that inflammation. And so I think being able to target IRF5 in IBD really helps get at that particular

component of inflammation that's really important in ulcerative colitis, and will lend itself to potentially combining with other mechanisms that go beyond those particular pro-inflammatory cytokines if you want to be able to tackle multiple different aspects of the pathophysiology of a disease like UC or Crohn's. So, I think that's the beauty of it.

I think the other aspect is the potential safety profile of IRF5, and being able to knock IRF5 down hard, and not really having there be risk of infectious complications, that also will lend itself to combinations.

Joseph Catanzaro:

Great. Thank you.

Stefan:

Thank you. Our next question will come from Jeet Mukherjee with BTIG. Please unmute your line and go ahead.

Nello Mainolfi:

Great. Thanks for taking the question. Maybe coming back to the market opportunity for KT-621. Nello, before you mentioned you're looking to mobilize patients on the sidelines because they aren't ready for an injectable, could you maybe put some numbers or quantification around how big that population is on the sidelines due to needle aversion or phobias around that, particularly in atopic dermatitis? Thanks.

Nello Mainolfi:

Yeah. Yeah. I mean, and to be clear, I don't think what's driving that is needle phobia. I mean, there is a percentage of it. I think it's probably relatively a small percentage. I think most of it is, again, it's the barrier to an advanced systemic injectable therapy that both prescribers and patients have for just accepting or feeling like there is a need of having a protein injected in your body for a disease like atopic dermatitis. I think that's really what's blocking people for transitioning from topicals into advanced systemic therapies.

And the numbers are out there. If you just talk about AD, there's probably 40 million patients with moderate to severe AD, but maybe it's easier to do ... We have the number of 50 million that includes also other type 2 inflammatory diseases. So really only almost less than two million patients have received dupi, lebri, nivo, Rinvoq in these diseases. So, some companies do the math differently, but those are the numbers. If you look at diagnosed moderate to severe patients, we're talking about tens of millions of patients. If you look at treated patients with this advanced systemic therapy, we're talking about less than two million. So that's the opportunity, and that's far greater than, for example, the opportunity in psoriasis these days. So, I think it's really hard actually to put the value e on ‘621 right now. I think a lot of us are being quite conservative for a good reason. We're still relatively early in the development of the drug, but I believe strongly that post this Phase 2b data, we need to get much more,

I think, aggressive with what we're really talking about. And I think maybe that would be a good time to talk about more discrete numbers.

Nello Mainolfi:

Okay. Thanks folks.

Stefan:

Thank you. Our next question will come from Sudan Loganathan with Stephens. Please unmute your line and go ahead.

Sudan Loganathan:

Thank you. Good morning, Bruce, Nello, and Jared. My question is on the ‘621 program for asthma and related downstream indications. As we get our first look at asthma data in the late 2027, does that outcome dictate readthrough and investment in going forward with COPD and other related indications? And also, are there any other go, no-go decisions much like this coming in the next 12 months as we start seeing more data for ‘621? Thanks.

Nello Mainolfi:

Yeah, no, I think, as we said, thank you for multiple times. It's really about dose selection. We hope to be able to take the Phase 3 dose that we'll use in asthma in other diseases. We have absolute confidence that this drug will work in all type 2 diseases. So, we're really waiting for the Phase 3 dose that will come out from the Phase 2b asthma study.

Sudan Loganathan:

Thanks.

Stefan:

Thank you. And our next question will come from Kripa. Just one moment, please. Sorry.

Yep. Our next question will come from Kripa Devarakonda with Truist. Please unmute your line, turn on your video, and ask your question.

Anna Li:

Hi, guys. This is Anna on from Kripa. Thanks for taking our question. Just one question on ‘621. I know you haven't disclosed the doses that you're going to be pursuing, but I was just wondering if you could give us a sense of the dose response range you're hoping to show with the three doses.

Nello Mainolfi:

Yeah, so I don't think we're going to get into it. I think we always think about the opportunity to explore a lower dose in which you'll see a less activity for both mechanistic and regulatory reasons, and then obviously a dose that will be optimal to move forward within the three doses. And so that's how we're thinking about the dose selection.

Anna:

Thanks so much.

Stefan:

Thank you. Our next question will come from Brian Abrahams from RBC.

Nello Mainolfi:

Operator let's try and move more quickly. All right, thank you.

Brian Abrahams:

Hey, guys, thanks for taking my question. So on '579, as you think about optimizing its therapeutic window, you mentioned you're going to be looking at degradation and some of the biomarkers. Anything specific that you're going to be looking out for on the side effect side there, just based on the mechanistic or preclinical data? Is it just overall suppression of the immune system or any other things that IRF5 or the other IRFs may be involved in metabolism or epithelial cells, et cetera? Thanks.

Nello Mainolfi:

Thank you. So based on preclinical data, we really haven't seen in animals, at least, adverse events of meaningful impact, or any actually. And so the question is always this theoretical infection risk. We know that all the IRFs are contributing to pathogen surveillance, and so we believe that removing only one should not have an impact on that. So, I think that's what we'll see obviously as things progress, but we don't expect any particular adverse event here with this drug of note.

Brian Abrahams:

Thank you.

Stefan:

Our next question will come from Tazeen Ahmed with Bank of America. My apologies. We now have Derek Archila from Wells Fargo. Please unmute your line and go ahead.

Hau Shen:

Good morning. This is Hau calling in for Derek, and thank you for the question. So, we were at AAD and we also hear KOL noting KT-621 is the most promising candidates in AD. A question on the efficacy. I

think they wanted perfect safety. On the efficacy side, I think we are hearing that even if it's less effective than dupi, some of them point to 70% as effective, others using Otezla as example, they will still be very excited. So, I guess my question is what you are hearing, what's enough to really mobilizing those patients with not on biologic, but be open to this oral option?

Nello Mainolfi:

Yeah, I mean, you've said it. I think I agree with you, and obviously we've heard the same things, which is you don't need to have biologics like efficacy to mobilize millions of patients from a topical therapy. Again, the only reason why we keep pointing to a Dupi-like profile is because this is the data we've seen so far. But if we end up seeing less, I think this could still be a huge drug in the space.

Hao Shen:

Awesome. Thank you so much.

Stefan:

Thank you. Well, that's all we have time for questions for now. So, I'll now like to turn the call over to Nello Mainolfi for closing remarks.

Nello Mainolfi:

Well, thanks everybody. I'm sorry we kind of ran out of time, and hopefully we didn't leave anybody behind, but we're always available to take more questions offline. Thanks again for following us and for all the engaging questions and see you soon on the next one.