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PRESENTATION

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

All right. Good morning, everybody. So it's very much my pleasure to start off the day today with Pfizer's head of R&D, Mikael Dolsten. It's very much my pleasure to welcome him. And Ronen Tamir from Investor Relations is going to start off with just the brief disclaimers.

Ronen Tamir *Pfizer Inc. - VP, Investor Relations*

Thank you, David, and good morning. I just want to make sure that we are all aware that today, we're going to make some forward-looking statements, which are true for today, and the actual result might change materially. And I encourage all of you to look at our SEC filing for the full forward-looking statement and disclosures. Thank you.

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

Wonderful. Well, Mikael, thank you very much for being with here -- with us here. We very much appreciate it. I thought it would be helpful just for you to set the stage on Pfizer's R&D spending overall. Obviously, the company has gone through transition and has rationalized, refocused, acquired Seagen. But I think setting the stage would be a good place to start, and then we can go from there.

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

Yes. Thank you, David. Always a pleasure to be with you here.

And we spend according to our general statements, in this year about \$11 billion to \$12 billion. And as you know, our revenue base is approximately, I mean, maybe \$60 billion, so that gives you a sense. It is -- we are trying to become more efficiently, like every company in every division. So while we have reduced somewhat compared to if you would have added just Pfizer and Seagen, this has been part of our continuous improvement process.

It's still one of the largest R&D budgets in the industry, in total. I am responsible for 4 of the 5 research and development areas. So my team executes end-to-end vaccines, internal medicine, immune inflammation and infectious diseases. We also support, through some of the heavy tech platform that we carry, design of small molecules in oncology, safety, medical support in certain aspects. So it's an organization that contains deep platforms and certain disciplines that are focused on therapeutic areas.

In total of the 11 to 12, we are spending on programs about 60% on the 4 areas that I lead and about 40% on oncology programs.

QUESTIONS AND ANSWERS

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

Excellent. And with respect to your activities, let's turn to what's exciting. So what are some of the programs that you're most excited about and that we should be focused on?

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

Yes. Let me put it into what I call the scientific key value drivers, what are they right now. The first one, it's a legacy strong area, bacterial vaccines. While we have quite recently got our 20-valent novel pneumococcal vaccine approved for adult and pediatrics, we're already moving a fourth-generation conjugate vaccines that will contain more serotype and also improved technology forward.

We know, as you and others point out, this is an area where more companies are coming in. We have been leading it for -- this is our third decade. So while we defend it vigorously, we also have added growth drivers in bacterial vaccines, among them *C. difficile*, where we

have made some great progress and look forward to see that drive bacterial vaccines to new heights.

The second one is the seasonal vaccines that are the more viral vaccines, where, of course, our COVID business is, with continuous upgrades of that. We have added a flu vaccine that's now in a combination with COVID in a Phase 3 for younger adults. And we have our recently launched RSV vaccine for 2 indications that also have a significant expansion program that we can talk more about.

The third pillar would be in internal medicine, where we have some efforts on various aspects of weight regulation in human disease. One is cachexia, where I think we are pioneering some efforts, and it's an area increasingly more in need because of many chronic conditions, whether cancer, heart failure, COPD or aging. And we have ponesegromab that we think could be a multibillion-dollar asset across cancer, cachexia and also heart failure.

Of course, in internal medicine, we have our obesity platform that now lies on 3 different assets, of which one of them is -- has gotten a lot of attention, danuglipron, where we're now working on a once-daily formulation after having concluded a Phase 2 trial earlier on a twice daily. We have other assets in the broader cardiometabolic setting that are in the clinic.

And then I would mention benign hematology. It's an area where we started with hemophilia, and we have added sickle cell disease. And we believe that area will be a very significant growth for us. Initially, we launched, through the acquisition of GBT, Oxbryta that's doing well. We are coming with a follow-on drug, 601, and we have several assets in hemophilia that are now in very late stage of registration, marstacimab, that we think will be approved this year, hemophilia B gene therapy in registration, and hemophilia A reading out likely in the middle of the year or so.

So those were 5 examples of large growth drivers. We sometimes use the term they can drive mega blockbuster value, which we have defined as \$3 billion, plus. But actually, I think each of these 5 can drive much bigger value because it relies on multiple pillars and contain already well-established franchise choices that we expand.

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

Excellent. That's a great framework. And we only have 22 minutes more, so I don't know how we're going to go through all that, but I'll do my best. So with respect to the vaccine readouts ahead, so what should we be watching and when?

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

We'll soon have a readout for the RSV 18 to 59 years, and that gives us the opportunity to expand from all 60 plus, to those that have comorbidities, which is pretty common nowadays, unfortunately among younger people and play an important role. It's the widest age span of any of the vaccine players that could then reach for the fall season.

And of course, we recently shared 2 season data that will be published with -- which looked really good, strong. And otherwise, we have the -- in addition to RSV the modFlu data, the Phase 3 trial that's ongoing that is also reading out this year, and it's also in the younger adult population that we think will benefit from combination vaccine to vaccinate frequently for flu, they vaccinate less frequently for COVID, which by combining the 2, we think will improve public health and hopefully bring it to similar level that you see for the older adults. So these are, I would say, some of the things really happening this year in the seasonal vaccine area.

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

And with respect to modFlu, could you just talk about influenza A versus B coverage and what you had updated on last year and what to watch in the coming months? I think the readout is coming relatively soon for that trial.

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

Yes. This is the -- we call it the second generation modFlu that is combined with the COVID. The first generation showed that the mRNA platform when used properly can be very powerful, as it was an event trial that we said was superior to standard of care. And to the best of my knowledge, that hasn't been reported in recent time for any new vaccine in the 18 to 59 superior to standard of care.

Now that was an event trial, and we had basically a few, if any, B cases. And on immune response, our levels against B was lower than

standard of care. Of course, if outcomes contains more than antibody immune levels, but we have made some improvement, we formulated it and have now been able to show in Phase 2 that we have very robust immune response, not just to A, but also to B, although B is increasingly less common.

And actually, recently, it has been proposed that for next season, one of the B strain should be removed. It should be a trivalent vaccine to A1b. So we feel, because of the improvement, very positive about being able now to generate immune data that's strong for the 2A and the B that will be used. And we rely on previously robust superior efficacy for the primary end point.

So that tells me it's possible to make improvement in a disease that has been for a long time like flu, and we bring it together with the COVID. And what we see is that we can retain the good antibody response for COVID. So I think it can be a really nice improvement for the 2025 season when we hope to have it possibly approved in the U.S. and worldwide.

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

And just so I understand the timing. What was the timing of pivoting to the newer version with the better B coverage?

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

We have been running this event trial over a couple of seasons, so it's part of our continuous efforts to put in new science. And the mRNA platform is an area where we at Pfizer constantly improve the mRNA string, the LNPs and how we package the amount of RNA and LNPs.

And as we made the improvement, we transferred it to flu, and we could note in a Phase 2 trial that dose improvement had particular importance for the B strain. And as the trial from the event trial came, we thought this brings us an opportunity to take the best what we learned in the first and incorporate with new technology to have what we think could be a best-in-class and a first flu-COVID combo vaccine.

It is important. We've seen in pediatric sector that you improve vaccination rates when you come with combination vaccines. And we think that's going to happen now in the adult sector and allow us simplicity, convenience and access to larger population.

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

Excellent. And then you had talked about your pioneering work in cachexia. Could you talk about that a little bit more, please?

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

Yes. GDF-15 turns out to be a major factor driving a kind of sickness field and also catabolic metabolist, which means that you are losing weight, you have a poor appetite, poor nutrition status. And 20% to 30% of cancer patients, which means the major cancers, do die with cachexia contributing to disease.

So we have seen in an earlier smaller clinical trial that we could substantially improve how much they eat, their body weight, their nutritional and functional status. And we think it will be by itself improving long-term outcomes, and we'll make patients more fit for treatment.

And we are targeting initially some of the larger cancers that are driving these outcomes, among them, lung cancer and pancreatic cancer. And many regimens today, even those with the immuno-oncology product, contain chemo backbone, and this will improve the ability to stand through treatment and being in a better performance status.

We're also running in heart failure. We see similar cachectic phenotype. You also see it in COPD, which include that some of the muscles involved in breathing is becoming poor because of weight loss.

So we think it can be a pretty big area. It's kind of the 2 ends. Obesity have gotten all the attention, and we want to play there. But also, cachexia with an aging population and chronic diseases, we think there's a big opportunity to improve long-term outcome for patients.

It's a very convenient administrated antibody, and it has performed really well in clinical studies. So it has the potential to be simple and easy administrated with maybe a monthly interval for patients, depending on finalization of dose, et cetera.

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

And when are the next major readouts to watch?

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

We will have a -- the Phase 2 readout for cancer cachexia this year, and that could position us for potential to move to Phase 3, pending regulatory dialogue. And we're already in a Phase 2 trial with heart failure that could follow after that. And we are exploring, looking at COPD, just to give you some example of very big diseases where patients are suffering from this.

We have gotten interested in cachexia and also have other program that face what's called geriatric anorexia. The aging population start also to have cachexia as a major problem, limiting their lifespan as they're past 75.

And it's a growing population that will be a burden on health care and their own well-being. So we think this cachexia is a pretty big phenomenon with different component, whether you are an aging patient or a patient that suffer from chronic disease.

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

Excellent. That's great. So maybe we could pivot to the vision for obesity R&D. Obviously, you're working on the potential once daily for danu, but you have other efforts as well. So if you could just provide a framework and what to watch, both with respect to when you'll have clarity on the possibility of danu once daily and then other options.

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

Yes. First of all, we feel, given our skills in cardiometabolic that this is an area we are committed to. And our presence in global primary care over a long time position us well for that.

In total, we have 3 assets that are pure obesity in the clinic and another asset that works on muscle energetics that could also be a very interesting space.

Of the 3, 2 are GLP-1s and 1 is a validated mechanism for obesities through the peptide therapeutics that are used, and that's really our strategy. We use our unique skills to make oral, small, convenient, scalable, small molecule.

And based on principle that has been validated by injectable in this area, why do we think that's really attractive? Well, it's approaching 1 billion patients worldwide that suffer from obesity. And you have noticed it's really hard to bring manufacturing of peptides to that scale and the need to make devices doesn't make it practical for a broad population of overweight and obesity. The 1 billion is overweight and obesity, but that's really the segment that's addressable now, and the overweight often have then comorbidities, cardiovascular, renal, et cetera.

And with the lead asset that did deliver really robust body weight loss up to 13% over 36 weeks, danuglipron, we are working with a set of once a day sustained release formulations that will wrap up around midyear. We promised first half of the year. And we'll be able to look at that and define next steps.

We have strong skills in modified release and have brought many drugs into the market, and that makes me encouraged to believe that we can address the once a day challenge we put in front of us in a good manner, and look forward to get that data and review them and prepare for next step.

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

Excellent. So when you mentioned the 3 assets, obviously, one of them is danuglipron. But what are the other 2?

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

The second is another GLP-1 that has some different features also in the clinic and looks encouraging when it comes to PK and dose. And the third one, we haven't released the mechanism yet. But it's one of those mechanisms that's been validated by biologicals from companies that are in that space, the type of mechanism that you hear from Lilly and Novo. And we've been able, I think, by far, being the first company to make an oral version of it.

So while a drug like the GLP, danuglipron is a bit ahead as it would have strong number of patients in Phase 2, plus possibly a once a day that we'll discuss as we approach middle of the year, we could see that as a potential first entrant. The second drug would be a nice combination in order to build a portfolio that address different type of patients.

Some patients may need to lose 10% of body weight and be in a normal spectrum, and it addresses their metabolic dysfunction. Other patients may want to have more body weight loss and may need combo agents. And you really see that, now, from the peptide companies that they play with single, double mechanism of action. And we're making progress on a variety of different mechanisms, but these are the 2 more advanced and more to come oral version of peptide-validated mechanism.

And again, with this large population of obese patients, just in China, as an example, you have 600 million patients overweight and obese, and that's a place where an oral drug would thrive. Of course, in United States, too, where you may have 150 million patients that could be qualified, it would be very hard to satisfy all of those segments with just injectable. And that's why you see us and some other companies pushing into the oral segment to be able to access that larger population.

David Reed Risinger Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst

Excellent. So you've mentioned those second and third, those are both in Phase 1 currently.

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

The second and the third are both in Phase -- have concluded -- one of them had concluded Phase 1, is now gearing up for a Phase 2 trial. The second one is just concluding Phase 1. So it's moving pretty swiftly, that with 3 different assets.

David Reed Risinger Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst

So just to clarify. So the second GLP-1 is gearing up for Phase 2.

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

Yes.

David Reed Risinger Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst

And then the one that you haven't disclosed the mechanism for, that's wrapping up Phase 1.

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

No. It's -- the one that on -- the novel mechanism is already in planning for the Phase 2 study.

David Reed Risinger Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst

Okay. We had it in reverse.

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

(inaudible) and it looks like a low dose, well behaving, typical beautiful Pfizer oral drug. And the other GLP-1 beyond danuglipron is just concluding Phase 1, finalizing the cohort. But whether we and how we would develop that, of course, depends on danuglipron.

If we have a QD on that, we may be happy with that and not need the second one. On the other hand, we have seen that the GLP-1 assets play a role in metabolic disease. They may play a role in certain addiction diseases. They may play a role in certain neurological conditions. So we also thought it could be to our advantage to have more than one GLP and be able to combine them with other oral drugs that I spoke about.

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

Excellent. Yes?

Unidentified Analyst

The second GLP-1 that you have finished Phase 1 and are in Phase 1, how is that...

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

No. He mentioned it's the new mechanism that is...

Unidentified Analyst

The second he said it finished Phase...

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

We are wrapping up Phase 1, I said. We haven't...

Unidentified Analyst

That's the third one, you're wrapping up Phase 1. That's the mechanism you won't have or the second GLP that you told us should indicate a PK done Phase 1 and you...

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

We conclude in Phase 1. So we haven't...

Unidentified Analyst

What's the difference from danuglipron? How is that different?

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

Well, every...

David Reed Risinger *Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst*

Yes. For those -- there might be some on the webcast. So the question is for the second phase -- for the second GLP-1 beyond danuglipron that's wrapping up Phase 1, how is it different?

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development*

As I said, danuglipron is the lead drug for us because we have treated more than 1,500 patients, so we know it's safe. And our focus is to get to once a day.

The second one, I would, at this point, see more, like you see in all the obesity companies, they are developing multiple drugs for this area because it will be different needs for different type of patients. And this, we may not need a second one at all and decide that we're all fine.

There are areas like addiction, the various craving conditions outside body weight, there has been intriguing reports on neurological disease, some of the companies running trials in Parkinson and Alzheimer. So it gives us just one more card if ever needed. I would focus for now on danuglipron and..

Unidentified Analyst

Let's focus on danuglipron. You're finishing up your extended release study. We will have the results by midyear. What about safety? Danu's biggest problem was nausea, vomiting. It was very strong, very much. Is that improving with the extended release, especially one, the tolerability...

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

Yes. The safety is where you have issues that could stop the drug. Tolerability is how well it affects the patient.

Unidentified Analyst

Is tolerability improving for danu in extended release? That's the first question. Second question, your weight loss is still 15% with danu. And others are coming out with 20%. Like orforglipron would be 20, and others are claiming even higher. While these are coming out with once a day, why will anybody use danu long term?

David Reed Risinger Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst

Yes. So let me repeat the question. So the question is twofold. First, how is the extended release going to impact the tolerability because there were tolerability issues in the danu data? And then second, if it generates 15% weight loss, will it be competitive with others, orforglipron and potentially combos that could drive greater weight loss?

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

First of all, we only develop drugs beyond, of course, the early clinical development that we believe can be differentiated for patient and satisfied needs that are unique for patients, number one.

Number two is that if you look at, for example, data on semaglutide, which is more modest in weight loss maybe than Mounjaro at certain doses, it had dramatic effect on cardiovascular outcome in renal. So there is a balance between how much weight you lost -- lose and your general health. Too much weight loss leads to muscle impairment.

So I'm not sure we should be so simple and think more is always better. We need to look at the holistic taking care of patients, and GLP have effects that are beneficial beyond weight loss. So I wouldn't lock myself into a box and think about only that.

And when it comes to tolerability, please remember, we had forced titration in that trial in order to reach and really answer the question, can a oral molecule give 10% or more weight loss. That was our goal. And yes, it could. But it was forced titration.

If you look at some of the other studies where they go from forced to allowing physicians and patients to more individualized titration, it improves dramatically tolerability. So there are many ways that you can go from Phase 2 and onwards and improve tolerability.

And if you really look at the danu data compared to Altimune data and the BI data on the GLP glucagon, they are all in the same ballpark of nausea, vomiting, diarrhea. We just chose again it's a lot how you decide in a Phase 2 to generate data fast or have extensive durations of treatment up and down.

So I wouldn't focus on that. It's a safe, efficacious drug. Can we get it once a day? We put all data together and have the opportunity to discuss our next steps around media. Appreciate your interest, but I want to make sure also David can answer -- ask me more question and just to visit. It's one of our many interesting opportunities.

Unidentified Analyst

All right. Last question. The muscle growth, can you give us the mechanism of your muscle-sparing drug? And your growth hormones, others are looking at growth hormones for muscle-sparing for you.

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

Yes. I mean that's...

David Reed Risinger Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst

The question is on the muscle drug, could you provide more color?

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

So the question about muscle punctuates that you need to be careful in how much weight you lose too fast, because then you need to be on a muscle-sparing drug. And that's why I said maybe the future isn't just about adding more drugs because you got side effect, but rather how you use the drugs.

No, I will not disclose the -- it's an oral drug. It's more focused on muscle energetics, how muscle work than the typical growing muscle drugs that you're referring to. So it's going to be a different one.

Unidentified Analyst

Growth hormones only?

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

It's an evolving field, and I would just stay open and see how it -- but my primary thinking here is that if you can avoid losing too much muscle too fast, it's far better for the patients than worrying like you do how to rebuild muscle. Okay.

David Reed Risinger Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst

All right. Wonderful. So maybe we could just move to the fourth-gen PCV candidate. I think you mentioned that it would be adjuvanted. So could you talk a little bit more about its profile? And if it's adjuvanted, would it likely be specifically for adults rather than infants?

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

So we have developed bacterial vaccines, in general, a set of different adjuvants. For this fourth generation, we have not disclosed whether that particularly contains adjuvant or not.

So we have 3 different tool kits that we deploy on these bacteria conjugate vaccines. If needed, adjuvant and in contrast, the C. difficile vaccine that we're working on now, we have included an adjuvant in order to reduce the number of doses needed. And we think it's primarily used in an older population where you need quick to raise antibodies to protect them when they go into hospital or use antibiotics.

In the PCV, we have also introduced new conjugation chemistry, a new generation of chemistry that allow you to get stronger, better immunogens and antibody responses. And we're exploring more than one carrier, which means it's not just the (inaudible) proteins.

But we only want to give you those examples on how we continuously advance our tech platform and that we believe we can improve immune response against old serotypes to get them more effective and add more serotypes. And that's really the profile or the forced one, more serotypes than the 20 and improving for select serotype. And that brings what we think a new generation that can be very powerful and can be explored for infant and adults.

David Reed Risinger Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst

Excellent. Well, I think we're out of time. Thank you so much for being with us here today. Appreciate it.

Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President, Pfizer Research & Development

Thank you, as always. It's great talking to you, David.

David Reed Risinger Leerink Partners LLC, Research Division - Senior MD & Senior Research Analyst

Thank you.

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