FDA Media Briefing on the First Gene Therapy Approved in the U.S.
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Coordinator: Good afternoon and thank you all for holding. Your lines have been placed on a listen only mode until the question and answer portion of today's conference. At that time if you would like to ask a question please press star 1, please unmute your phone and record your name clearly when prompted.

I would like to remind all parties the call is now being recorded. If you have any objections please disconnect at this time.

And I would now like to turn the call over to Andrea Fischer. Thank you. You may begin.

Andrea Fischer: Thank you. Good afternoon. Thank you for participating in today's call. My name is Andrea Fischer and I am with the FDA's Office of Media Affairs. This is a media briefing to announce the FDA's approval of the first gene therapy in the U.S. By now the agency's news release for this announcement has been issued and posted on the FDA's website.

Today I am joined by Commissioner Scott Gottlieb and Dr. Peter Marks, Director of the FDA Center for Biologics Evaluation and Research. Commissioner Gottlieb and Dr. Marks will both provide remarks on today's action. Following their remarks we will move to the question and answer portion of the call.

Reporters will be in a listen only mode until we open up the call for questions. When asking a question please state your name and affiliation. Also please limit yourself to one question and one follow up so we can get to as many questions as possible.

I will now turn the call over to Commissioner Gottlieb.

Scott Gottlieb: Thank you for joining us today. Today is an important milestone in a long journey we've been on to transform clinical medicine by using modern advances in genomics. As one part of that journey researchers spent many decades working on technologies that could modify human cells and tissue using the tools of gene therapy. This was always held out as a way to alter the course of many vexing diseases and maybe even deliver the ability to cure some deadly disorders.

There have been many challenges on that path. We've witnessed hardships and even tragedy along the way. We've also realized certain triumphs. Today a pivotal leg in that journey is complete. The science has reached a point of superiority where enough of the components of these endeavors have worked out. We can deliver effective therapies to patients. We can deliver on the original promise.

FDA is announcing the approval of the first gene therapy product in the United States. FDA is approving the drug Kymriah for the treatment of certain pediatric and young adult patients with a devastating and deadly form of leukemia.

Many people have contributed to the science that made today possible. There are many patients who committed themselves to clinical trials that have enabled these opportunities to advance. There are many people at the company that developed this product: the drug maker Novartis who remain steadfast to a challenging and risky scientific vision. There are many people at FDA who worked for decades on defining a framework for properly

developing and evaluating these platforms while this field underwent intense scrutiny and setbacks.

And there are many researchers across the world who made incremental advances that all consolidated to give us this scientific moment: the opportunity to have his effective new therapy that will help young cancer patients and to change the face of modern medicine and drug development in the process.

Gene therapy products are now being studied in many diseases and conditions including genetic disorders, autoimmune diseases, heart disease, cancer, diabetes, and HIV/AIDS. At FDA we look forward to working with the research and development community to advance potential new therapies in these serious disease areas which affect millions of Americans and their families.

Today is just the first approval in this promising new class of medical products. Other similar medical opportunities lie just behind this milestone. To give you just one example related to the Agency's current action, FDA has granted more than 550 active investigational new drug applications related to gene therapy products and has 76 active investigational new drug applications related to CAR-T cell products. Providing patients with timely access to advances in medical products is a critical component of FDA's work. We're committed to expediting the development of new and groundbreaking therapies that have the potential to be lifesaving.

Towards these ends today's review and approval of Kymriah happened quickly. It's being approved seven months after the FDA received the application. The approval also involved the cross agency approach in which the FDA's top oncologists and gene therapy experts worked together to help

ensure Kymriah would be available as quickly as possible. This program alignment is an organizational approach that we intend to pursue more widely at FDA across other therapeutic areas as a way to improve our efficiency and deepen our scientific collaboration.

I'd like to personally thank the FDA staff and leaders in the Center for Biologics Evaluation and Research and the Oncology Center of Excellence for their collective efforts to make today possible. They work to pioneer and implement this more collaborative scientific model for drug review at FDA.

Today's announcement was many years in the making. At FDA we're committed to doing our part to help advance breakthrough science that has the potential to deliver outside benefits to certain patients who aren't served well by conventional therapies. In the coming months FDA will be advancing new policies to help make the development of very novel technologies more efficient.

I will also continue to advocate for policies that improve access to these treatments. Today my colleague at the Centers for Medicare and Medicaid Services, Administrator Seema Verma will take steps to facilitate this access by pursuing more novel approaches to coverage of these kinds of highly targeted, highly specialized therapies.

I want to close by thanking you for joining us today as we move forward together to unlock the full potential of gene therapy for patients. I'd like to introduce Dr. Peter Marks, Director of FDA Center for Biologics Evaluation and Research, the FDA center that is tasked with regulating cellular and gene therapies.

Peter Marks: Thank you Dr. Gottlieb. Today's approval of the first gene therapy in the United States represents a remarkable advance in treating serious and life-threatening diseases. Although gene therapy has been on the horizon in the United States for about two decades many challenges had to be overcome leading to the approval of the first such therapy.

Such a novel and innovative approach is a development of chimeric antigen receptor T cells, or CAR-T cells for short, required collaboration from across the research and development communities with contributions from academic researchers, the pharmaceutical industry, government agencies, treating physicians, and most importantly the patients themselves.

Generally gene therapy involves changing the genes or genetic makeup of a cell in order to cure or treat disease. For example a gene therapy might replace a defective non-functioning gene that causes a serious disease with a healthy copy of that gene that would either treat or cure the disease. Regarding today's approval, CAR-T cells are a form of gene therapy as the patient's T cells are genetically modified to enable them to recognize and destroy cancer cells.

A simplified description of how some CAR-T cells are made and how they work to treat cancer is that white blood cells are removed from the patient using a specialized process and then T cells are isolated from the pool of white blood cells. A genetic construct is then introduced into the T cells using a special type of virus designed for this purpose. This places genetic material encoding an antibody grafted onto a T cell receptor into the cell and then the cells are grown outside of the body to get sufficient numbers to give back to the patient to treat the disease.

When the CAR-T cells are given back to the patient following treatment with chemotherapy to reduce the number of lymphocytes the new genetic material

that has been introduced directs the T cells to bind to and kill the cancer cells that have the right target on their surface. This use and others of CAR-T cells may turn out to be more broadly applicable and they're being studied in other settings to treat solid tumors, certain infections and autoimmune disease.

Gene therapies hold a great deal of promise. There is tremendous activity in this field at the time as evidenced by the fact that FDA is actively reviewing over 500 investigational applications for gene therapies, including those for CAR-T cells. Still we have a good deal to learn about how these products work, how to administer them safely, and whether they will continue to work properly in the body without adverse side effects.

Along with academic, industrial and other government partners at FDA we're working to better understand the safe and effective application of gene therapy. This includes conducting applied research in our laboratories to better understand how they can be manufactured and given safely and working towards optimizing clinical trial designs that will facilitate their evaluation.

We will continue to do everything within our resources to help academic and other investigators as well as pharmaceutical companies advance development programs in order to bring such important treatment to patients in need. This includes making full use of our expedited development programs such as breakthrough therapy designations and regenerative medicine advanced therapy designation whenever possible.

In this regard I want to thank my colleagues at FDA's Center for Biologics, Evaluation and Research and at the FDA's Oncology Center for Excellence for their outstanding work in interacting with the company during the entire development process and moving forward this groundbreaking approval well ahead of the goal date. We look forward to working with the research and

development communities to continue to make innovative therapies available for patients who need them.

Thank you for joining us today. I'll now turn the call back to over to Andrea.

Andrea Fischer: Thank you Dr. Marks. At this time we will begin the question and answer portion of the briefing. When asking a question please remember to state your name and affiliation. Also please limit yourself to one question and one follow up so we can get to as many questions as possible. Operator, we'll take the first question.

Coordinator: Thank you and as a reminder to ask a question please press star 1.

Our first question today is from (Dennis Thompson).

(Dennis Thompson): Hi. Thank you for taking my question. I was just wondering do we have any idea at this point how much this therapy is going to cost patients?

Scott Gottlieb: We're going to refer questions about the pricing to the company and to Medicare as well. They have that information.

(Dennis Thompson): Thank you.

Andrea Fischer: Great. Operator, we'll take the next question.

Coordinator: Thank you. Our next question is from (Jeanine). (Jeanine), your line is open.

(Jeanine): Hi. Thanks for taking it. Can you tell us a little bit more about the risk evaluation and mitigation and about the certification requirements for doctors who want to use the therapy?

Peter Marks: So this is Peter Marks. So the product was discussed in an advisory committee and was carefully considered and a process was put in place to ensure that the institutions that use this product will have the availability of the treatments that are necessary for cytokine release syndrome, one of the major complications that can occur that are associated with the therapy and that that will be readily available when the treatment is given.

There are other provisions that have - that are put in place so the doctors are properly trained in how this will be used and essentially institutions that will be using this are ones that are going to be familiar with the use of such drugs.

(Jeanine): And as a follow up can you talk a little bit about the post-market studies that were a condition of approval, i.e., how long, how many patents, and what will you be looking for specifically because the release of it was based on just that 53-patient trial. So just curious about that.

Peter Marks: So of course there will be a post-market study done and I think we can get back to you with details of that by email. So I - we'll get back to you on that.

Andrea Fischer: Operator, we'll take the next question but folks please remember to state your name and affiliation when asking a question.

Coordinator: Thank you our next question is from Lynne Peterson.

Lynne Peterson: This is Lynne Peterson from Trends-in-Medicine. There would (unintelligible) details later but details through all of the…

Andrea Fischer: Hi Lynne. Your line is breaking up a little bit.

Lynne Peterson: I'm sorry. I'm in Spain and (unintelligible).

Andrea Fischer: Okay we could hear you then.

Lynne Peterson: Okay. So the question is will you please send details on the post-marketing study to all of the callers, not just to the person that posed the question? We're all interested in that. Clarify (unintelligible) excuse me. Clarify the comment you made about (unintelligible) involved in this (unintelligible) process has already started (unintelligible) of this. Is it a parallel (unintelligible)…

Andrea Fischer: Lynne I'm sorry. We'll take the next question. Lynne, we can follow through an email since you're breaking up to us. We can't hear your question.

Coordinator: Thank you our next question is from Peter Loftus.

Hi this is Pete Loftus from the Wall Street Journal. Dr. Gottlieb or Dr. Marks, you spoke about the potential additional applications of this and there's a lot of studies underway. But is there any particular uses that you would single out as being more promising and perhaps more eminent than others? And then secondly can you provide more details about the CMS arrangements that you referred to?

Peter Marks: So I can start. This is Peter Marks. I think that it's a matter of what studies have been conducted to date that would indicate where there's the most data available and for right now the other studies indicating the potential for CAR-T cells to have greatest promise are in the area of (hemologic) malignancies including adult forms of leukemia, both the acute and chronic types and certain types of lymphoma, Non-Hodgkin's lymphomas. But again those that are not yet - obviously not yet approved and are investigational.

Scott Gottlieb: Peter this is Scott Gottlieb. I'd refer you to CMS on the second question. My understanding is they're going to be issuing some documents later that will explain what they intend to do in this setting.

Andrea Fischer: Okay Operator, we'll take the next question.

Coordinator: Thank you and as a reminder to ask a question please press star 1. Our next question is from Denise Grady from New York Times.

Denise Grady: Hi thank you for taking my question. I'd like to ask you please, the risk evaluation and mitigation strategy with these elements to ensure safety use: is this a first or an unusual step to have this level of certification and these requirements for the use of a drug? Is there any precedent for this?

Peter Marks: There certainly is precedent for these types of strategies when we consider there to be risks that could be mitigated by proper education of physicians. For instance in other drugs, for instance there have been educational strategies that have been required for physicians as well as patients. And in this particular case this particular risk mitigation strategy is one that's helped to - that we believe will help ensure the safe use of this product in patients.

Denise Grady: Is it unusual though? I mean, how common is this to try to put it in perspective?

Peter Marks: I think it's difficult for me to say how unusual it is in this setting. I would just say to you that in this particular case when you have a highly effective therapy and you have drugs that are available that can potentially mitigate one of the side effects reasonably effectively the package together made a lot of sense.

Scott Gottlieb: And we can get back to you with some other examples. There are certainly other drug approvals where we've had similar measures put in place at the time of approval. So it's not - there's nothing unprecedented about the kinds of measures that are being adopted in these setting.

Denise Grady: Okay good.

Andrea Fischer: Operator, we'll take the next question.

Coordinator: Thank you our next question is from Nick Florko from Inside Health Policy.

Nick Florko: Hi thanks for taking my call. Can you please outline some of the uncertainties that FDA may have grappled with before ultimately deciding to approve the product and what the Agency did to mitigate those concerns?

Peter Marks: So much of this I think going back to Dr. Gottlieb's remarks this approval builds on essentially decades of work in the area of gene therapy to ensure that the vectors that are used for this are as safe as they possibly can be, that the technology that is being applied is as well understood as it could be. In this case FDA looked at the vectors that were being used to ensure that they seem to be as safe as they possibly could be and in terms of minimizing the ability of something called replication competent retroviruses from redeveloping out of this. We looked at the process of giving this, of manufacturing very closely.

So basically each step from making the cells to how they are - were given to patients and the entire process, the treatment of the side effects were evaluated in determining how this could be approved.

Scott Gottlieb: When you think about the sort of scientific inflection that created the opportunities a lot of things happened along the way. I think one of the most

tangible and meaningful was the ability to come up with competent, safe, effective vectors to deliver the gene therapy products. That was a key turning point in this field.

Peter Marks: And I guess the - that - just to amplify on that this has been even in the field of CAR-T cells over the past decade there has been an advance where there have been several different generations of these and this current generation is an improvement over the previous generations.

Andrea Fischer: Okay. Thank you. Operator, we'll take the next question.

Coordinator: Thank you. Our next question is from Michelle Cortez from Bloomberg News.

Michelle Cortez: Thanks so much for taking the question. I'm curious about CAR-T more broadly. I know that the next therapy that we have coming up isn't requiring an FDA - an advisory committee meeting and I'm wondering if that is a reflection of the CAR-T space and how much advances we've had here or if it's a reflection of the disease itself. I'm just wondering how comfortable you are moving forward with this very novel technology which you guys alluded - or, you know, spoke about very movingly but in terms of it's still just hundreds of patients. So I'm wondering what we can think about going forward from the regulatory perspective, how closely you need to track every step here. Thanks.

Peter Marks: You know, I can't speak to other products at this point. I can speak to this one that we're talking about today.

Andrea Fischer: All right Operator, we have time for one more question.

Coordinator: Thank you our final question today is from Andrew Siddons from Congressional Quarterly.

Andrew Siddons: Hi thanks for taking the questions. I'm wondering: do you think that the Agency has the resources to make sure that Novartis follows through with its follow up study? The GAO found last year that the FDA didn't have resources to always make sure that the companies who were required to do post-market follow up studies were able to complete them. Do you think that's changed since then?

Peter Marks: Let me say from the standpoint of my position as Director for the Center for Biologics Evaluation and Research: I believe that we certainly do have the resources to make sure there's appropriate follow up and follow through on this and we intend to make sure that that's the case. But I'll also turn it over to Dr. Gottlieb in case he wants to add any (unintelligible).

Peter Gottlieb: Yes I'll just echo that. I feel very confident we have the resources to do this postmark and oversight and I think it's essential - and this is a priority of mine: I think it's essential that we make sure a company's affiliate post-market commitment is an essential feature of making sure that we can approve products through these new pathways such as breakthrough - the breakthrough pathway we're under accelerated approval, we have to make sure companies if they're going to have the advantages of those pathways to fill the commitments that are part of those policies.

Andrea Fischer: All right.

Andrew Siddons: Thank you.

Andrea Fischer: That's - thank you for joining us today. As a reminder the FDA's press release can be accessed on the FDA's Web site. This concludes today's media briefing. A replay of this call will be available in about an hour and will be up for 30 days. Thank you.

Coordinator: Thank you and this does conclude today's conference. You may disconnect at this time.

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