

**FDA Media Briefing on the first gene therapy approved in the U.S. to target a disease  
caused by mutations in a specific gene  
Dec. 19, 2017  
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Coordinator: Welcome, and thank you for standing by. At this time all participants are in a listen-only mode until the question and answer session of today's conference. At that time, you may press star one on your phone to ask a question.

I would like to inform all parties that today's conference is being recorded. If you have any objections, you may disconnect at this time. I would now like to turn the conference over to Ms. 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 approved in the US to target a disease caused by mutations in a specific gene, and to provide an update on gene therapy. By now, the agency's news release for this announcement has been issued and posted on the FDA's website.

Today I'm joined by Commissioner Scott Gottlieb and Dr. Peter Marks, Director of the FDA's Center for Biologic Evaluation and Research. Commissioner Gottlieb and Dr. Marks will both provide remarks on today's call.

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 the call up 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: Thanks a lot. And thanks for joining us today. As we approach the end of what's really been a landmark year in medicine I'd like to reflect on the intersection of policy and science that's opened new paths for the discovery and development of innovative technologies to treat and cure disease in ways that just weren't possible a short time ago.

We're at the inflection point - an inflection point in medicine and health where we're witnessing now the advent of brand new technology platforms that have the potential to improve health and cure disease in fundamentally novel ways. Applications like gene therapy and regenerative medicine may cure inherited disorders and rejuvenate damaged cells and organs.

And tools like digital health applications and more sophisticated diagnostics have the capability to more fully empower consumers with information to tailor their medical care and inform them about their treatments. With each of these and similar novel products, the novelty of the technology that the FDA's being asked to evaluate challenge the agency to adapt its usual approaches to product regulation in some new ways.

We need to make sure that we're taking policy steps to enable these innovations to efficiently advance to benefit patients while we maintain our gold standard for ensuring the safety and efficacy of new products. The approval today of the first directly-administered gene therapy is especially notable.

Not only for what the new treatment does and how it works -- by engineering a virus as a vehicle to deliver the gene directly to its target inside the body -- but also for how we've expanded the use of gene therapy beyond the treatment of cancer to the treatment of vision loss for children and adults.

Today's action reinforces the potential of this innovative technology in treating a wide range of challenging diseases. And we're taking steps to extend the opportunities offered by gene therapy. We recently announced our comprehensive policy framework for regenerative medicine, including a draft guidance that describes the expedited programs that may be available to sponsors of these gene therapy products.

To expand similar policy efforts, when it comes to facilitating the advance of gene therapy, next year we'll begin issuing a suite of disease-specific guidance documents on the development of specific gene therapy products. These guidance documents will be a part of a modern, comprehensive framework for how we'll help advance the field of gene therapy while making sure that new products meet FDA standards for safety and benefit.

These policies will articulate -- among other things -- new clinical measures to develop - for the evaluation of gene therapy for different high-priority diseases where the platform's currently being targeted. These new documents will address clinical areas where there is a lot of interest in using gene therapy techniques, such as certain more common single-gene disorders.

And we intend to provide innovators with clear advice on safe and effective development pathways, including potential accelerated approval endpoints. The spirit of these efforts was embodied in the review of this new gene therapy product today for the treatment of an inherited form of vision loss.

We recognize that with novel therapies for some of the most vexing diseases and conditions often comes a need for new clinical measures to allow these technologies to go forward. In this case, it meant the validation of a new standard that will help guide the development of future therapies that address severe vision disorders.

Our Office of Tissue and Advanced Therapies -- which had familiarity with the issues involved in the study of products for vision loss -- recognized that showing differences in visual loss and visual acuity might be difficult. In this review, the FDA suggested and worked with the product sponsor to develop and validate a new, more practical endpoint that could reflect true clinical benefit in both pediatric and adult patients instead of relying on only visual acuity or visual field testing.

Other similar medical opportunities to the one that's being approved today lie just behind this milestone. To give you just one example related to the agency's current approval action, there are more than 600 active investigational new drug applications related to gene therapy products.

And researchers at the Massachusetts Institute of Technology estimate that about 40 gene therapies might win approval by 2022 from a current pipeline of 932 development candidates. They estimate that about 45 percent of these relate to treatments for cancer. I can't confirm their estimate, but I can affirm that we're at the early stages of a transformation in medical care as a consequence of these and other transformative platforms.

I want to thank you for joining us today as we move forward to unlock the full potential of gene therapy for patients. Now I would like to introduce Dr. Peter Marks, the Director of FDA's Center for Biologics, Evaluation and Research - the FDA Center that's tasked with regulating regenerative medicine

including gene therapies -- to talk more specifically about today's approval action. Thank you.

Dr. Peter Marks: Thank you Dr. Gottlieb. Today's approval of the first gene therapy in the United States that treats an inherited disease caused by mutations in a specific gene signals, another exciting development in the field of gene therapy. This marks the third gene therapy approved by the FDA since late August, and represents another key milestone in bringing these important products to patients.

Gene therapy involves changing the genetic makeup of a cell to treat or cure a disease. For example, a gene therapy might replace the defective, non-functioning gene that causes a serious disease with a healthy copy of that gene. Gene therapy could also involve repairing a malfunctioning copy of a gene or interrupting the function of a gene that is causing problems.

These changes could either treat or cure the disease. Another form of gene therapy involves reprogramming a patient's own cells to have new properties that enable them to have new functions, such as recognizing and destroying cancer cells.

The two CAR-T Cell products approved in later summer and fall -- Kymriah and Yescarta for examples of this type of gene therapy. Today's approval -- Luxturna -- is what many concern - consider to be a traditional form of gene therapy. It's a virally-vectored gene therapy where viruses are modified so they don't cause disease and are used to carry therapeutic genes into human cells.

In this case, the product works by delivering a normal copy of a defective gene directly into retinal cells. These retinal cells then produce the normal

protein that converts light to the electrical signal in the retina to restore a patient's vision loss.

In contrast to the previous approvals -- which were for what we are essentially calling personalized cell-based gene therapy products -- today's approval is for a gene therapy product that can be given directly to an individual to treat a disease.

Gene therapies hold a great deal of promise. Gene therapy products are being studied in many areas including genetic disorders, autoimmune diseases, heart disease, cancer, diabetes, and HIV/AIDS. We look forward to working with the research and development community to advance potential therapies for patients in these serious disease areas.

Still, we also 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. At FDA -- like our colleagues in academia, industry, and other government agencies -- 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 given safely, and working toward optimizing clinical trial designs that will facilitate their evaluation. It also includes making full use of our expedited programs such as breakthrough therapy designation and regenerative medicine advanced therapy designation wherever possible.

As Dr. Gottlieb noted, critical to this approval was the work done by FDA with the manufacturer to develop an innovative clinical endpoint used to evaluate Luxturna. Specifically, we worked with a product sponsor to develop

and validate an endpoint that could be used in both pediatric and adult patients that involve the negotiation of a standardized maze-like obstacle course under different amounts of light.

The illumination ranged from 400 lux -- which is consistent with an office environment or food court amount of light -- down to one lux -- which is consistent with the amount of light from an indoor nightlight or what you would see on a moonless night. The test was scored for accuracy and time.

This multi-luminance mobility test -- or MLMT -- was the endpoint developed to demonstrate clinical benefit in the clinical trial that evaluated the efficacy and safety of this new product. In some cases, the results for those treated with the gene therapy were quite dramatic.

I'm very proud of our review staff's effort to work with the product sponsors to identify a solution that demonstrated a meaningful effect for patients. I'd like to thank my colleagues in FDA's Center for Biologics Evaluation and Research for their outstanding work in interacting with a company during the entire development process and moving forward this groundbreaking approval well ahead of the application's 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 over to Andrea.

Andrea Fischer: Thank you Dr. Marks. At this time, we will begin the question and answer portion of the briefing. As a reminder 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. If you would like to ask a question, please press star one, unmute your phone, and record your name clearly. If you need to withdraw your question, press star two. Again, to ask a question please press star one. It will take a few moments for questions to come through. Please stand by.

Our first question comes from Sue Sutter with The Pink Sheet. Your line is open.

Sue Sutter: Hi. Thanks for taking my question. On this issue of the suite of guidances that are going to be coming out next year on gene therapy, are any of those going to be dealing with some vision loss conditions? And if so, are they going to be recommending this novel end point that (unintelligible) developed for Luxturna.

Scott Gottlieb: Yes, we -- Sue, this is Scott Gottlieb -- we haven't commented yet specifically which clinical areas we would address. So we're not going to go beyond that right now. But we would expect to be able to speak more - in more detail about that early in the new year.

Andrea Fischer: Great. All right...

Sue Sutter: Okay, thanks.

Andrea Fischer: ...yes, no problem. Operator, we'll take the next question.

Coordinator: Our next question comes from Kate Sheridan with Newsweek. Your line is open.

Kate Sheridan: Hi. Thanks again for taking my question. I'm wondering if you think that the experience working through the approval process with Luxturna will be instructive if and when a gene editing base treatment is submitted for evaluation?

Dr. Peter Marks: This is Peter Marks. So I think that each one of these approvals that we've had has helped us understand more thoroughly the types of evaluation both in terms of the manufacturing process that we have to evaluate, in terms of the controls that have to be in place, and in terms of the clinical monitoring after someone receives the therapy that will need to be in place.

So I think that this is helping the agency develop increasing amount of knowledge that will help us as we go through and deal with further products that come in. Obviously every new product will have some new challenges or new aspects to it. But I think that -- as we build knowledge in this area -- it will help us ease the way for new products as they come in.

Coordinator: And again -- as a reminder -- you can press star one on your phone and record your name if you have a question. One moment please for any additional questions. We may have a question coming in, one moment please. The next question comes from Susan Schackman with CBS News. Your line is open.

Susan Schackman: Hi, this is Susan Schackman. There was some quote about the cost of the drug. Can you address that? We've seen up to a million dollars.

Peter Marks: You know, I can't speak to that. And the - to my knowledge the company has not formally announced the cost of this. So I think questions on the cost should be directed to the firm.

Susan Schackman: Thanks.

((Crosstalk))

Coordinator: And again...

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

Coordinator: Thank you. And again, to ask a question at this time you can press star one on your phone and record your name when prompted. One moment please for any additional questions. We are showing no further questions at this time.

Andrea Fischer: All right, thank you. If we have no further questions, we'll go ahead and wrap up. Again, thank you for joining us today. As a reminder, the FDA's press release can be accessed on the FDA's website.

This concludes today's media briefing. A replay will be available in about an hour and will be up for 30 days. Thank you.

Coordinator: So this concludes today's conference. Thank you for your participation. You may disconnect at this time.

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