FDA STATEMENT

Statement by FDA Commissioner Scott Gottlieb, M.D., Director of FDA's Center for Drug Evaluation and Research Janet Woodcock, M.D. and Director of FDA's Center for Biologics Evaluation and Research Peter Marks, M.D. on Expanded Access –Looking Forward

For Immediate Release:

March 29, 2019

Statement From:

Commissioner of Food and Drugs - Food and Drug Administration
Scott Gottlieb M.D.

For more than 30 years, the FDA has supported patients' access to investigational medical products for treatment, outside of participation in a clinical trial, when appropriate. The FDA remains deeply committed to this effort. Helping to facilitate access to promising medicines for patients with serious or immediately life-threatening diseases or conditions when no comparable or satisfactory alternative therapy options are available is a high priority for the agency.

We cannot know in advance whether a drug obtained through expanded access (EA) will provide a benefit for these patients who have no other FDA-approved treatment options and cannot enroll in a clinical trial. But such access can often represent a patient's final hope for a potentially effective treatment. For the mother with breast cancer, it may lead to extra time to attend a daughter's graduation or offer a father with ALS the chance to be at his son's wedding. Maybe such access can lessen suffering in the last few months of a patient's life. Or maybe it enables a child with a rare and fatal disease to live many more years. Fostering these opportunities are among our most critical obligations.

Since 2010, drug sponsors and manufacturers have given the opportunity of such access to more than 13,000 patients. The FDA applauds those companies. While pharmaceutical development is ultimately a business, health care is about people's lives. Companies that innovate to develop effective new treatments show their commitment to the patients their drugs can potentially help

by providing such access. The willingness of many sponsors to provide their products to patients at no cost or at the cost of manufacturing is a testament to their action on this public health commitment.

As addressed in the preamble to our 2009 regulations, use of investigational drugs in treatment settings generally involves careful balancing that considers (i) the interests of patients with serious or immediately life-threatening diseases, who need to be able to make decisions about their health care, including using experimental therapies; (ii) the need to protect potentially vulnerable patients from unacceptable risks; and (iii) society's interest in ensuring that treatments for these diseases are developed and approved for marketing to enable broad access.

But sometimes, even in circumstances where the availability of a medicine through EA would appropriately balance these considerations, such access is not available. This is often true when it comes to the ability of patients to continue to use a promising medicine after the completion of a clinical trial.

We are writing to encourage sponsors to offer EA in such circumstances, when continued access to a promising medicine at the completion of a clinical trial would be appropriate under the EA programs.

Although we often focus on EA as providing access to patients who cannot enter clinical trials, EA can also be considered as a mechanism for those who have participated in a trial in order to allow them to continue receiving a drug that may have provided benefit. At the end of a trial, sponsors may continue to provide treatment to participating patients through an extension study to gather additional rigorous information that's needed to support the subsequent marketing application. Alternatively, if the purpose is primarily to provide the drug to patients who continue to need it, an EA program may be used for either moderately sized populations (intermediate EA) or large size populations (treatment EA), often when most studies in support of approval have been completed. As another option, a sponsor could authorize a patient's own physician to obtain a single patient EA investigational new drug (IND) application.

Once a trial is complete, EA is generally available when clinical trial results show that the drug is effective in the studied population. However, sometimes drugs that have not shown benefit across the overall study population may still be providing benefit for individual patients.

In such situations, EA may have a role in allowing patients to have continued access to the drug. We would generally support such efforts. Providing EA to patients who undertook the risks that are inherent to participating in any clinical trial is an acknowledgement of the contribution these patients have made to the overall drug development program. Of course, in situations where an experimental treatment is potentially associated with substantial risk -- and where the

therapy has not been demonstrated to be effective in a trial -- continued access must be carefully considered by the physician and the patient, and weighed by the sponsor, especially if further development of the drug is being reconsidered.

As mentioned previously, we know there are other considerations. A decision about whether to allow EA is weighed against the potential impact on the development program; the primary goal of any drug development program must be to expeditiously bring the drug to the market, thereby providing broad access to patients who need the drug. Many novel therapies are being developed by small companies that may have only a single product. The supply of investigational product may only be sufficient to support the clinical research trials, and not be adequate to support EA. In addition, certain biologics, such as cell and gene therapies, are particularly complex and expensive to manufacture, so the cost to the company of providing such access may be prohibitive.

Of course, financial challenges and concerns about the impact on the development program may not be the only barriers. There are persistent misperceptions among pharmaceutical companies about the risks of providing a drug under EA, despite evidence to the contrary.

We want to reassure sponsors that providing a drug under EA very rarely impacts development timelines. We urge sponsors to consider EA in appropriate settings; and especially after patients who are showing promise on an experimental drug complete therapy in a clinical trial setting.

An FDA analysis of more than 10,000 EA applications from 2005 to 2014 shows that the incidence of a clinical hold due to an adverse event on an EA IND was 0.2 percent compared to 7.9 percent for clinical holds for all commercial investigational drug development programs. The two cases of clinical hold resulting from an adverse event in an EA IND occurred in response to the deaths of two cancer patients, who were receiving treatment under different EA INDs, shortly after infusion of the investigational drug. In both cases, the clinical holds were resolved. In addition, a review of more than 300 regulatory decisions between 2010 and 2016 shows that EA did not result in a negative decision on any application. In only one case did a final label include a drug interaction based on EA experience alone. The FDA reviewers understand that assessment of any serious adverse event that occurs during EA must consider the context in which the investigational drug is provided, as described in our guidance.

It's very rare that EA impacts a clinical development program in a negative way. In addition, while perhaps not commonplace, EA may add to the evidence for approval.

For example, in the study on regulatory decisions discussed above, it was noted that the approval of uridine triacetate was based solely on experience within EA (60 single-patient INDs and 1 treatment protocol). In 2018, Lutathera (lutetium Lu 177 dotatate) was approved for the treatment of gastroenteropancreatic neuroendocrine tumors (GEP-NETs) based in part on data

from over 1,200 patients who received Lutathera at a single site in the Netherlands, initially through an EA program. These are not the only examples where information from EA programs was combined with information from clinical trials and supported approval decisions.

EA has been an important program, providing access to innovative therapies that can provide meaningful benefits to patients with serious diseases who lack therapeutic alternatives and cannot participate in clinical trials. We support efforts by sponsors to offer promising medicines to patients through EA. This includes continued access after the completion of a clinical trial, sometimes through an extension study. While EA may not be feasible in every situation, concerns about regulatory risks are often overstated. Such concerns are not supported by the data. At the same time, information from EA has sometimes proven valuable, contributing to the overall data available about a drug that is included in the marketing application.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

###

Inquiries

Media:

Amanda Turney (mailto:amanda.turney@fda.hhs.gov)

301-796-2969

Consumer:

888-INFO-FDA

More Press Announcements (/news-events/newsroom/press-announcements)