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April 18, 2024

Dr. Terence Flotte, M.D.
Provost and Dean, UMass Chan Medical School
Vice President, American Society of Gene and Cell Therapy
122 Paxton Road
Holden, MA 01520

Dear Dr. Flotte:

Thank you for appearing before the Subcommittee on Health on Thursday, February 29, 2024, to testify at the hearing entitled "Legislative Proposals to Support Patients with Rare Diseases."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on Thursday, May 2, 2024. Your responses should be mailed to Emma Schultheis, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to Emma.Schultheis@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Brett Guthrie
Chair
Subcommittee on Health

cc: Anna Eshoo, Ranking Member, Subcommittee on Health

Attachment

Attachment — Additional Questions for the Record

The Honorable Brett Guthrie

1. Your testimony suggests some need for the FDA to exercise a degree of regulatory flexibility in its process for trials of rare disease treatments or drugs. In a scenario where a treatment or drug was developed, and has shown safety and efficacy for one rare disease in Phase 1-2, but also shows promise for wider application, should there be such flexibility to proceed with the original purpose as a primary endpoint even while adding targets to test for wider application?
    a. In addition to your testimony, advocacy for such flexibility appeared in two published submissions to the New York Times in the days leading up to the hearing.
        i. Links:
            1. Opinion | Gene Therapies Could Transform Rare Diseases. Are We Holding Them Back? - The New York Times (nytimes.com)
            2. Opinion | Three Mothers' Plea to the F.D.A.: Save Our Children - The New York Times (nytimes.com)
    b. Following up, can you comment on the breakthroughs in gene therapy for cystinosis and whether the risks and opportunities described in your testimony may apply to this rare disease's treatment, currently making its way to Phase 3?

2. Dr. Flotte, in your testimony you talk about running clinical trials involving a very small number of pediatric rare disease patients. You highlighted that we need to ensure that we have the right regulatory processes in place for these unique situations. As I understand it, there are actually individualized, or so-called "N of 1" therapies being developed and that the equivalent of the FDA in the UK recently launched a pilot program "to develop a pathway for children with rare conditions to access therapies made specifically for them." Do you have any thoughts the UK's Rare Therapies Launch Pad and whether this type of development and review pathway is something that we should be considering in the U.S.?
    a. Link:
        i. Pilot launched to support children with rare conditions to access… (genomicsengland.co.uk)

The Honorable Robert Latta

1. How does a bill like the MINI Act further precision/personalized medicine so that the right patient receives the right treatment, at the right time?

2. How can we also ensure that the IRA's price setting construct does not impact the ability of other highly innovative drugs, such as cell and gene therapies, to come to market?

3. I am glad to see more attention paid to ensure ALS patients are able to get specialized care from Medicare providers. This is an extremely important aspect of any ALS diagnosis – getting timely treatment to extend the quality of life for as long as possible.

Can you comment on how well FDA is doing at engaging with new ALS treatments and moving those through the approval process? While the FDA work is ongoing, are they becoming available for trial?

4. What do you see as the potential for greater use of the vouchers over the next five years to incent drug development for pediatric rare cancers such as brain tumors?

The Honorable Gus Bilirakis

1. Your testimony discusses the recent scientific advances in cell and gene therapies, and with your background in pediatrics I'm sure you see the daily quality of life issues these patients and their families face. While we await more game-changing technologies coming to market, I hope we don't also lose sight of the fact that pediatric patients need new treatments to lower their disease burden now. Products that improve their daily life, that lower the amount of steroids and other harsh drug regimens they are currently forced to take on, or ones that have fewer side effects, also deserve the FDA's undivided attention. That's why we should be streamlining the FDA's processes when it comes to rare disease, and we should ensure that FDA incorporates patient-experience data into their benefit-risk assessments. I am proud to cosponsor the BENEFIT Act, which will ensure FDA incorporates this data in its benefit-risk assessments. Would you agree that FDA should take this into account, and can you tell us the importance of incorporating real-world evidence in clinical trial settings?

2. Oftentimes, securing funding for rare disease research can be difficult, particularly for cell and gene therapies, and orphan drug development is often more costly and lengthy than non-orphan therapies. How has the prospect of receiving a rare disease PRV attracted funding for rare disease drug development?

3. As you know, 95% of the 10,000 known rare diseases currently do not have any FDA approved treatment. Considering the dire need to have safe and effective therapies for rare disease patients, how important is it to have the correct incentives in place for companies to research rare diseases, especially for children?

4. Why does it take time to see the impact of a policy like the rare pediatric PRV?

5. Will providing an additional four years allow for a more robust evaluation of the rare pediatric PRV program's impact?

6. The FDA's review process is often inconsistent between its many review divisions, which has a negative impact on companies trying to develop new therapies. What can be done to help make FDA's review processes more consistent and predictable while still maintaining their emphasis on safety and efficacy?

7. In January of this year, FDA Commissioner Califf called for "creative approaches" for rare disease therapies, as the current pathways are not optimal. What are some specific

ways that the FDA can exercise regulatory flexibility to allow rare diseases therapies to be evaluated quickly?

8. I was a proud co-lead of the TRANSPLANT Act, which was enacted in 2021 and reauthorized the C.W. Bill Young Cell Transplantation Program and the National Cord Blood Inventory, which provides thousands of Americans access to lifesaving treatments made possible through the use of cord blood. For over thirty years, cord blood cells, collected from the umbilical cord after birth, have been used in transplants to treat over 80 serious diseases, including rare diseases such as sickle cell, thalassemia, Krabbe disease, metachromatic leukodystrophy (MLD), severe combined immunodeficiency (SCID), Gunther disease (CEP), Hunter syndrome (MPS II), Niemann-Pick disease, and an array of immune deficiencies. Continued research into the use of cord blood as a source material for manufacturing various types of rare disease treatments is evolving rapidly, leading to new innovations that have the potential to save lives and offer children impacted by these life-threatening diseases a new hope at life. How have you seen the use of cord blood in treatments improve the lives of children with rare diseases?

The Honorable Anna Eshoo

1. As advanced cell and gene therapies are approved by the FDA to treat adults, additional support is needed to spur similar innovation and investment in gene therapies to treat rare pediatric diseases. That's why I introduced the Creating Hope Reauthorization Act to provide incentives for research and development of new drugs to treat rare pediatric diseases.
    a. How can we ensure children aren't left out of the new frontier of medicine in cell and gene therapy?