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Oral Statement to the Institute of Medicine Committee on Accelerating Rare Disease Research and Orphan Product Development

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Good morning. My name is Sara Radcliffe. I am Vice President for Science and Regulatory Affairs and Acting Executive Vice President for Health for the Biotechnology Industry Organization (BIO). BIO represents more than 1,200 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations.

On behalf of BIO members, thank you for holding this meeting and for your inquiry into the effectiveness of existing strategies to promote research discoveries and development of orphan products to improve the health of people with rare diseases.

As this Committee is well aware, more than a quarter-century ago, Congress passed the Orphan Drug Act (ODA), which contained several incentives for biotechnology and pharmaceutical companies to develop products for rare diseases. The ODA has been an enormous success. In the decade prior to enactment of the ODA fewer than ten products for rare diseases came to market. Today, according to FDA, there have been 344 applications for orphan indications approved for marketing. These products have helped millions of people in the US and around the world.

I'm proud of the contribution the biotechnology industry has made to this field over the years. Indeed, the mission of many biotech companies is to bring hope to the patients who suffer from rare diseases.

Despite our successes over the years, though, there are still an estimated 6,000-7,000 rare diseases for which there is no treatment. These diseases afflict about 25 million people in the US, as well as another 25-30 million in the EU. Many of these diseases are serious or life threatening. It's clear that we have much more work to do.

BIO believes that the lesson we can learn from the ODA is that government policies can effectively foster research and development of products for rare diseases. The challenges of

developing orphan products are great and they require innovative policy and regulatory solutions. Further, many rare diseases affect far fewer patients than the 200,000 threshold in the ODA. For these diseases, the challenges are even more daunting.

Today, I would like to briefly share with you our thoughts about policies that will complement the ODA and facilitate the development of the next generation of orphan products. I also will be submitting a longer, written statement for the record.

BIO's ideas include: policies specifically designed to support or incentivize research and development; improvements in FDA regulatory policy; and reimbursement for off label use of products.

The ODA created a grant program administered by the FDA to fund companies for development of orphan products. It's called the Orphan Drug Grant Program. This program has not had increases in funding commensurate with inflation for many years. BIO urges increased funding for the Orphan Drug Grant Program. I also note that in Europe, orphan products receive 10 years of market exclusivity, while only receiving 7 years of exclusivity in the US. Given its importance, we urge consideration of a longer US exclusivity period to coincide with Europe.

In addition, NIH launched the new $24 million Therapeutics for Rare and Neglected Disease (TRND) program this year. Though just getting off the ground, the TRND program has the potential to help companies bring promising products forward. Many of these products stall in development because biotech companies lack the financing to advance them. The TRND program could fill some of these funding gaps.

BIO is encouraged by this effort. We pledge to work with the NIH on intellectual property concerns, technology transfer rules, and other matters to make sure the program accomplishes its goals.

BIO companies believe that FDA has made great strides to make sure that safe and effective orphan products reach patients as soon as possible. For example, we applaud the FDA Office of Orphan Products Development for their sponsorship of the training program for reviewers on statistical methods for small patient populations. In addition, the recently-announced program "Build an Orphan" – designed to help companies properly submit the application for orphan drug designation in a timely fashion – holds promise. But more must be done.

Similar to what FDA has done through its Critical Path initiative, we believe the agency needs to take affirmative steps to spur drug development for rare diseases. The regulatory approval pathway simply must be more predictable.

For example, during the most recent negotiations surrounding enactment of the Prescription Drug User Fee Act (PDUFA), the FDA committed to developing a series of guidances regarding clinical trial design; adaptive clinical trials; and new methods of statistical analysis. These would be valuable for developers of rare disease products. Unfortunately, these guidances have still not been published.

In addition, we urge FDA to publish additional guidance regarding orphan drug development that provides interpretation of current regulations including: what are acceptable subsets of disease to meet the prevalence requirement; what is a "major contribution to patient care" that allows a drug to be found "clinically superior" even if it has the same active moiety of a previously approved drug; and whether the sponsor of the original drug can also be a "subsequent sponsor".

Other regulatory changes should be pursued as well, such as greater transparency at the agency including more meeting opportunities, and greater consistency among FDA's review divisions. Moreover, we request that the FDA support alternative clinical trial designs as well as use of surrogate clinical endpoints for studies of rare disease products. Changes such as these will help companies access the accelerated approval process – which is often not used for rare disease products.

The bottom line is that the challenges of developing rare disease products require new regulatory approaches.

Finally, under current rules, off label uses of drugs and biologics are not reimbursed by insurers. Unfortunately, many of the products taken by patients suffering from rare diseases are labeled for another indication. The lack of reimbursement often impedes access to these products and in turn, provides a disincentive for companies to develop them.

BIO encourages the IOM to recommend use of compendia to determine whether an orphan product should be reimbursed if prescribed off label. This would be analogous to the current treatment of cancer products. To get listed in a compendium, the manufacturer must provide data regarding safety and effectiveness of its product for the off label indication.

Use of compendia will allow patients suffering from rare diseases timely access to new therapies and encourage innovation. They ensure patient access to the latest drugs and biologicals for medically accepted uses. These policies also encourage innovation and continued research by giving patients a choice of new therapies, recognizing new uses of therapies, and promoting a relatively stable and predictable reimbursement environment. As you may know, this is critical for many of our member companies who depend on private sector investment.

In sum, BIO companies' mission is to develop innovative products to meet unmet medical needs. Many of these products are for patients suffering from rare diseases. Despite our progress, far too many patients with these diseases still have no treatments. We look forward to working with this Committee, the Congress, FDA, NIH, patient advocacy groups, and other stakeholders to enact policies to speed the development of much-needed therapies.

Thank you for your time and consideration of this important topic. I am happy to answer your questions.