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The Honorable John Shimkus
Energy & Commerce Committee
2452 Rayburn House Office Building
Washington, DC 20515

Dear Representative Shimkus:

Thank you for the opportunity to provide additional information regarding the Subcommittee on Health hearing entitled, "21st Century Cures: Modernizing Clinical Trials."

1. You state in your testimony that "advances in next generation sequencing, imaging and molecular diagnostics (e.g. proteomics) are contributing to our understanding of how and why drugs may have different effects in different individuals with the same diagnosis." In what ways can such genomic sequencing and molecular diagnostics help support subpopulation drug and device development?

Advances in next generation sequencing, imaging and molecular diagnostics enable us to study, in greater detail, a disease process and the response to therapy in individual patients. When these advanced tools are used to study populations with what appears clinically to be the same disease, they often allow recognition of different subpopulations of patients with somewhat different disease processes at the molecular and cellular level. This testing and recognition can lead to the discovery of drugs specific for a subpopulation (i.e., targeted therapy), and facilitate the clinical testing of targeted therapeutics.

With regard to discovery, when a pathophysiologic process is found to be prominent in a subpopulation of patients, one has a clue that targeting that process may lead to discovery of a valuable intervention.

In clinical trials, use of biomarkers and imaging agents enables one to identify and study patients with the specific process being targeted. A study focused on those patients most likely to benefit or least likely to be harmed is more likely to be beneficial to participants, has increased probability of success, and, in some cases will have lower costs and shorter timelines. When a drug's use is limited to the population most likely to benefit and/or least likely to be harmed, the risk-benefit profile will likely be far better than when it is used more broadly.

Several innovative clinical research designs have been developed to make use of biomarkers and imaging modalities in clinical research. For example, a broad collaboration between FDA, industry, not-for-profits, and academic researchers has developed Lung-MAP, a master protocol for studying several drugs in advanced squamous cell lung cancers. In this study, use of biomarkers in patient screening informs treatment choices for initial patients, and learning from the ongoing trial about which patients respond best to which treatments informs treatment choices for subsequent patients. The goal is a more cost-effective and efficient process for identifying effective treatments.

2. What types of barriers do you believe Congress needs to address to ensure that the potential of precision medicine can be realized by both developers and clinicians?

I mentioned a number of barriers to realizing the potential of precision medicine in my testimony. First, electronic health records (eHRs) have enormous potential to inform clinical care. For precision medicine, eHR registries of patients could serve as a critical tool to identify subpopulations and target their treatments, particularly if the eHRs included, or were supplemented with, patients' genomic, proteomic, and imaging profiles. However, significant barriers to such use include the lack of standardization and quality control for eHRs, lack of interoperability of her systems, needed development of methodology re eHR data use, and the need for educating clinicians on the value of eHRs and incentivizing their use. Additionally, the process for obtaining consent and approvals for use of de-identified eHR patient data with minimal or no risk to the patient could be simplified while maintaining protection of privacy and rights.

Second, clinical trial networks created and governed by broad consortia, as mentioned in the response to question 1, can be a very valuable tool for clinical research in precision medicine. However, the numbers and reach of such consortia and networks are limited. Government, especially FDA and NIH, can play an important partnership role in creating and governing such networks; Congress should encourage and support those efforts. Patients, academics, and companies also will bring important insights and capabilities.

Third, a barrier to including a large, diverse, broadly representative group of patients in clinical trials is the lack of public education about the value of participation in clinical research while dispelling common misperceptions.

Three additional areas that would benefit from Congressional attention to aid in the realization of the potential for precision medicine are described below:

1. FDA has made progress in improving its coordination and internal collaboration in the regulation of targeted therapeutic agents with diagnostic tests, but more needs to be done. We suggest that Congress continue to encourage FDA's development of a consistent, efficient, transparent and coordinated regulatory pathway for these products.

2. With advances in the science behind precision medicine, the use of a diagnostic that optimizes the use of a drug in a subpopulation is quickly becoming a key tool in patient therapy. Current reimbursement policies for novel diagnostics that are used in precision medicine do not reflect the potential benefit they can bring to patients and the healthcare system. Congressional attention could help ensure appropriate reimbursement and market access.

3. Full realization of the potential of precision medicine will require continued and robust scientific innovation, and we would welcome Congressional actions to increase incentives for innovation that advances precision medicine.

Thank you for your consideration.

Sincerely,

ANDREA MASCIALE

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On behalf of

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