LUNGEVITY
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September 11, 2018

The Honorable Scott Gottlieb, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
[Submitted Electronically]

Re: **Patient-Focused Drug Development: Collecting Comprehensive and Representative Input Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders**

Dear Commissioner Gottlieb:

On behalf of LUNGevity Foundation, the nation's preeminent lung cancer nonprofit that funds research, provides education and support, and builds communities for the 234,000 Americans diagnosed with lung cancer each year and the 541,000 Americans living with the disease, we appreciate the opportunity to submit our comments in response to the "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders" issued by the U.S. Food and Drug Administration (henceforth, referred to as the Agency) in June 2018.

As a leading patient advocacy group that represents the voice and interest of the national lung cancer survivor community by accelerating research to patients that is meaningful to them, empowering patients to be active participants in their care and care decisions, and helping remove barriers to access to high-quality care, LUNGevity applauds the Agency for developing the first guidance document for all stakeholders involved in the drug development process. The document, first in a series of guidance documents, is an excellent starting point to educate stakeholders on the true principles of patient-focused drug development (PFDD) and provide tactics to adopt these principles throughout the drug development life cycle. The guidance series implements new requirements under 21st Century Cures Title III Section 3002 and new commitments the Agency made under the 2017 reauthorization of the Prescription Drug User Fee Act under Title I of FDA Reauthorization Act of 2017.

We would like to take this opportunity to share some of our own experiences with our patient preference study as well as comment on areas that may benefit from more clarity or direction. Our comments focus on: making patient-focused drug development truly patient-centric; providing a clear voice to the caregiver in the elicitation of patient experience; maintaining relevance of patient preference studies in an era of evolving standards of care; defining "representativeness" of lung cancer patient experience; conducting patient experience studies outside of a clinical trial

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setting; offering guidance on fit-for-purpose data; leveraging existing data sources; and describing a clear role for the payer.

A. Making patient-focused drug development truly patient-centric

LUNGevity Foundation has spearheaded the first lung cancer advocacy-driven patient preference initiative. The initiative, *Project Transform*, is a multi-year, multi-stakeholder collaborative endeavor between LUNGevity and Ohio State University. It encompasses core principles of patient-centered outcomes research (PCOR), in line with LUNGevity's mission of providing a voice to the lung cancer patient. The goal of *Project Transform* is to change the paradigm in lung cancer from assumptions being made about patients' wishes to evidence-based conclusions about patients' need and desires. Currently in its third year of a nationwide patient preferences survey, the project built its quantitative phase through a rigorous patient engagement model in which lung cancer patients provided direct feedback and input on the project implementation.[1,2] Drawing from the principles of community-based participatory research,[3] *Project Transform* has leveraged the expertise of lung cancer patients and caregivers right from developing the research questions to the construction and dissemination of the quantitative survey – using a bottom-up approach for patient preference research and gathering patient experience data.

While the Agency acknowledges the role of patients as experts, we encourage the Agency to provide more clarity on how patients and/or their caregivers can be involved in the conceptualization of the patient experience research project, from identifying meaningful attributes and psychometric measures to disseminating the results of the study. Such a participatory model provides an active role to the patient and/or their caregiver rather than a discrete study participation role, which, while important, does not holistically draw from the expertise of the patient and caregiver community. Furthermore, investing in this type of a bottom-up approach upfront may help mitigate problems such as participant recruitment and issues associated with sampling bias. In a healthcare reimbursement landscape where the burden of cost is increasingly shifting to patients, they [patients] are being "consumers" in the truest sense. Therefore, patients should be at the forefront of patient preference study designs.

B. Providing a clear voice to the caregiver in the elicitation of patient experience

Caregivers, defined as people who provide care to cancer patients who need help taking care of themselves,[4] play an important role in the treatment journey of a lung cancer patient, especially given the high symptom burden of stage IV lung cancer,[5] the poor prognosis of a lung cancer diagnosis,[6] and stigma associated with the disease.[7] A caregiver is often charged with managing day-to-day activities of a patient, including driving a patient to their doctor's appointment or to their clinical trial study center.[8]

Soliciting the caregiver perspective in the creation of a patient experience map is of paramount importance to capture the patient perspective. Evidence shows that a treatment approach that significantly improves the quality and length of life of a lung cancer patient is bound to impact a

caregiver. We encourage the Agency to provide direction on best methods to elicit and incorporate caregiver feedback.

C. Maintaining relevance of patient preference studies in an era of evolving standards of care

The lung cancer treatment landscape has rapidly evolved over the past five years, with the Agency approving more than 15 new treatments for advanced-stage non-small cell lung cancer (NSCLC) — more than in the prior 15 years combined. Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, diagnosed in about 85% of people with lung cancer.[9,10] The complex nature of this disease requires personalized management plans for patients.[10] Since the discovery of the first epidermal growth factor receptor (EGFR) mutation in lung cancer in 2004, targeted therapies have become a major component of the treatment arsenal of NSCLC patients.[11-13] Now at least 10 driver mutations in adenocarcinoma have been identified — EGFR, ALK, ROS, RET, ERB2/HER2 mutations, ERB2/HER2 amplifications, MET amplifications, MET mutations, TRK, BRAF, KRAS.[14,15] In concert with the identification of an increasing number of targetable mutations is the development of novel, potent, and more specific targeted therapies. For example, the first-line treatment options for EGFR and ALK positive lung cancer has changed in the last year. Furthermore, even for those NSCLC patients without a driver mutation, first-line immunotherapy with or without chemotherapy has become the standard of care.[16,17] This rapid evolution of care has increased the need to re-think patient preferences. Lung cancer patients are now living longer, higher quality lives.

Given this unprecedented progress we have seen in the treatment landscape of lung cancer, it will become necessary to re-evaluate patient and caregiver preferences, especially in discrete-choice experiments where comparator attributes are often derived from chemotherapy experiences. While it may be beyond the scope of the guidance document, we request the Agency acknowledge the importance of evolving standards of care in crafting patient preferences studies so that the studies maintain relevance for 4-5 years beyond the completion of the study. The need for maintaining relevance will become even more important as the concept of “comparative tolerability” enters the lung cancer space. A recent study of three PARP inhibitors in high-grade ovarian cancer demonstrated that while all three provided equivalent survival benefits, one of the inhibitors had a significantly lower toxicity profile than the other two. While the study was not designed to be a head-to-head comparison among the three drugs, it highlights the importance of quality-of-life measures (gathered through patient preference studies) in such situations where primary endpoints such as overall survival are met and may not differ dramatically across different therapies.[18] In such situations, patient preference data will be of paramount importance in determining appropriate care for a patient, where standard-of-care may evolve or multiple options exist.

D. Defining "representativeness" of lung cancer patient experience

We are grateful to the Agency for bringing up the importance of "representativeness", "representation", and statistical rigor. While "representativeness" and "representation" may be synonymous in some disease spaces, this may not be the case for lung cancer given the highly heterogeneous nature of the disease. The two sub-types of lung cancer are non-small cell lung cancer (85%) and small cell lung cancer (15%).[19] Non-small cell lung cancer (NSCLC) is further classified into adenocarcinoma and squamous cell lung cancer.[19] As described above, each of these subtypes of advanced-stage NSCLC have different treatment options available (based on the presence or absence of specific biomarkers), and those treatment options impact both quantity and quality of life of patients.[20] Similarly, treatment of extensive-stage small cell lung cancer is different from treatment approaches available for NSCLC.[21]

Patient experience research conducted within these different subtypes of lung cancer may not "represent" the lung cancer space but may still provide valuable insight and information that may be useful for drug development for these different subtypes of lung cancer. We request the Agency to provide clarity on how patient experience data useful to the Agency should be collected in a highly heterogeneous disease space such as lung cancer.

E. Conducting patient experience studies outside of a clinical trial setting

To date, most patient preference studies in lung cancer have been conducted within a clinical trial setting. In a systematic literature review of 20 patient preference studies conducted in lung cancer, only three studies used online market research companies[22] [23] and a patient registry[24] to solicit participants for their survey. As a patient advocacy group that represents the voice of lung cancer patients in the United States, we want to point out the importance of conducting patient experience studies outside of a clinical trial setting for several reasons.

1. Despite an expansion of clinical trials in global sites, an overwhelming proportion of trial participants are Caucasian (86% in 2014 vs. 92% in 1997).[25] Conducting a patient preference study within a clinical trial setting, while beneficial for submission purposes, is a missed opportunity for truly capturing the patient experience in a real-world setting, as the participant composition does not reflect the true prevalence of the disease in a real-world setting in different racial and ethnic communities. [26]

2. Furthermore, lung cancer clinical trials often exclude patients with brain metastases and low performance status.[27] Given that a majority of advanced-stage patients present with brain metastasis at the time of diagnosis or are very sick due to the high symptom burden of lung cancer, conducting patient experience studies within a pristine clinical trial cohort does not capture the lived experience of a lung cancer patient outside of a trial setting.

F. Offering guidance on fit-for-purpose data

We applaud the Agency for providing detailed guidance around qualitative and quantitative patient experience data and for recognizing the importance of social media as a vehicle for gathering information. The Pew Research Institute reports that two-thirds of Americans, under age 65, are Facebook users, reinforcing the importance of using informal platforms to gather patient experience data.[28] At LUNGevity Foundation, we have a very active social media community and currently moderate 14 lung cancer-specific Facebook groups. Members of these groups candidly share their experience on clinical trials, their current medication and associated quality-of-life issues, and side effect management. This can be extremely informative in conceptualizing and crafting a rigorous patient experience study and defining patient-friendly endpoints for a clinical trial. We encourage the Agency to provide a clear categorization of purpose of patient experience data and the level of rigor required for it. In our opinion, patient data that is not meant to accompany an IND submission may be collected through informal platforms as long as the objectives of the data gathering are clearly stated.

G. Leveraging existing data sources

We thank the Agency for the comprehensive nature of the guidance on prospective data collection on patient experience. Having said that, we would also like to remind the Agency that several organizations already collect observational patient experience data through established patient registries or annual surveys within their communities. According to the National Committee on Vital and Health Statistics, registries can be used for a broad range of purposes in public health and medicine as "an organized system for the collection, storage, retrieval, analysis, and dissemination of information on individual persons who have either a particular disease, a condition (e.g., a risk factor) that predisposes [them] to the occurrence of a health-related event, or prior exposure to substances (or circumstances) known or suspected to cause adverse health effects."[29] Consistent with this definition, patient registries can be extremely helpful with quality-of-life studies, outcome studies, post-market surveillance, and development of disease management guidelines, in addition to helping with recruitment for clinical trials.[30] It is common practice to consent patients prior to entering data into such registries and sharing their information. Furthermore, many of these registries are HIPAA-compliant, ensuring safety and security of patient data. Guidance from the Agency that provides a framework for using data collected retrospectively from such registries or establishing prospective registries that can collect patient experience data will be very helpful for patient advocacy groups.

H. Describing a clear role for the payer

While the guidance document provides a comprehensive overview of data collection methodologies as well as potential use of the data, it would helpful for the audience of the guidance document to understand how the document can be used by different stakeholders. While the patient and their caregiver, the treating physician, and the drug developers and

regulators may seem like the most likely stakeholders of such guidance, we encourage the Agency to also include language specific to payers. In a healthcare reimbursement landscape that relies on health technology assessment (HTA), payers are often stipulated to incorporate patient preferences in drug-value demonstrations.[31] U.S. payers may be increasingly compelled to adopt similar frameworks. Therefore, PFDD language that clearly pertains to payers, specifically how such information will be used for value-based frameworks, needs further clarification.

Again, we thank the Agency for giving us the opportunity to comment on such an important guidance document and applaud you for developing the first guidance document for all stakeholders involved in the drug development process.

The comments outlined above can be discussed with my staff, myself, and LUNGevity's Scientific Advisory Board, which is made up of some of the world's leading experts in lung cancer biology, practice management, access to innovative medicines, and overall patient care. I can be reached at 240-454-3100 or aeferris@lungevity.org if you have any questions or would like to engage in further dialogue.

Sincerely,

Andrea Stern Ferris
President and Chief Executive Officer
LUNGevity Foundation

ABOUT LUNGEVITY:

LUNGevity's mission is to improve outcomes for people diagnosed with lung cancer. Our goals are three-fold: (1) to accelerate research to patients that is meaningful to them; (2) to empower patients to be active participants in their care and care decisions; and (3) to help remove barriers to access to high quality care. We have the largest lung cancer survivor network in the country and actively engage with them to identify, understand, and address unmet patient needs. We also have a world class Scientific Advisory Board that guides the programs and initiatives of the organization. Additionally, we collaborate with other lung cancer patient advocacy groups and organizations, such as the American Lung Association and CHEST, who serve the lung cancer community.

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