October 31, 2012

Margaret Hamburg, M.D.
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD, 20993

Dr. Hamburg:

I am writing in reference to Docket no. FDA-2012-N-0967 addressing patient-focused drug development. First, I congratulate you and the FDA on this initiative. The patient perspective is critical, yet under-represented in the drug development process. This is particularly true in the area of risk. I recall quite clearly the comments of a young mother with Stage IV colorectal cancer when discussing the risk/benefit of a particular drug. She said, "I have little time left, and will not likely see my daughter turn two years old. This drug might give me some more time with her. I understand there is risk. But tell me the risk, and tell me the benefits, and let me decide." That the FDA is now creating a formal process to address this kind of patient engagement is an important step forward.

I encourage you to include melanoma as one of the twenty disease areas to be included in this initiative. As the largest and oldest non-profit working exclusively in melanoma, the Melanoma Research Foundation (MRF) interacts with patients and caregivers every day and the need for a better drug development process is clear. The current state of research and treatment for melanoma makes this disease a particularly compelling candidate:

Epidemiology: The incidence of melanoma is increasingly rapidly, particularly among young women where it is the leading cause of cancer. The average age of melanoma diagnosis is 50, much younger than cancer in general; this results in a larger loss of life years and productivity than might otherwise be expected.

Molecular Biology: The understanding of how melanoma forms is growing rapidly. We know that this disease is actually a cluster of several distinct cancers, each driven by different genetic mutations. The increased knowledge has resulted in the discovery of several potential targets for drug development, yet some sub-types of melanoma—particularly uveal, mucosal, and acral—have not been well incorporated into the discussions of drug development.

1411 K Street, NW Suite 800
Washington, DC 20005
(202) 347-9675
www.melanoma.org

Drug Development: In 2011 two new drugs were approved for treating metastatic or unresectable melanoma, after a gap of thirteen years in which no drugs were approved. Many more agents—intravenous, oral, and intralesional—are on the horizon. Given the breadth of treatments to be reviewed by the FDA in the near future, incorporating the patient perspective in this process will be consistent with PDUFA V. This perspective is particularly important given the number of Phase III studies soon to be underway, and the challenges in navigating the treatment landscape.

Drug Combinations: Melanoma experts agree that the most promising clinical approaches will involve combining two or more drugs together. This is supported by recent data published in the *New England Journal of Medicine* (N Engl J Med 2012; 367:1694-1703, November 1, 2012) showing significantly improved outcomes for patients treated with a combination of a BRAF inhibitor and a MEK inhibitor, vs. either drug used as monotherapy. Patients are asking for more combination studies to be done, yet many challenges remain, including uncertainty about toxicities. As this approach to care develops further, the patient perspective of risk vs. benefit will be vital.

Recent advances are encouraging but have not significantly extended overall survival for patients with advanced melanoma. More effective treatments are likely to be available in the clinical setting within the foreseeable future, but several issues remain unresolved. What are the best options for the 50% of melanoma patients who do not have the BRAF mutation? Why do targeted therapies work very well, but only for a short period of time? What are predictors of response to the new promising immunotherapy drugs? What risk and benefit is likely to come with various drug combinations? In all of these areas, melanoma patients can, should, and must be part of the conversation.

Because of the unique status of melanoma diagnosis, care, and drug development, this cancer is an ideal candidate for inclusion in the FDA's patient-focused drug development initiative.

Regards,

Tim Turnham, PhD
Executive Director

1411 K Street, NW Suite 800
Washington, DC 20005
(202) 347-9675
www.melanoma.org