September 11, 2020

Re: Public Comment on Docket No. FDA-2020-N-1529
for "Independent Third-Party Assessment of IND FDA-Sponsor Communication Practices in PDUFA VI"

Submitted to: U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20990

Warm Greetings to All at the FDA:

Following up on my oral testimony to the FDA delivered on August 11, 2020, this written public comment has a three-fold focus.

1. **Stage IV cancer care issues:** Spotlight on a stage IV cancer patient's story, which reflects common issues traceable to decisions made by the FDA at the IND stage (see subtitles *"Calling on the FDA to 'Put Patients First*" and "*My Mom's Preventable Pain*")
2. **The problem of surrogate endpoints:** The need for fuller, more rigorous understanding on the part of the FDA about human suffering, fatalities, and worsened health outcomes linked to increased use of surrogate endpoints, which are a substitute for more meaningful research outcomes about drug safety and efficacy (see *"Patient Stories: Grassroots vs Astroturf"* and *"Who's Accountable to Cancer Patients?"*)
3. **The need for patient-centeredness in FDA's communication at IND stage:** A current lack of accountability to grassroots patients in IND phase communication at the FDA —and the need for transparent, open-door processes inclusive of patients and their caregivers, beyond the otherwise closed-door negotiations between FDA and industry sponsors of investigational new drugs (see *"Bringing Our Truths Together"*)

I write to you as both an individual whose family was affected negatively by the use of surrogate endpoints, and as a board member of the USA Patient Network. USAPN is a coalition of grassroots patients and advocates who have overlapping membership in various grassroots organizations, or are individually affiliated with the USA Patient Network. The majority of our advocates have been trained through a grant funded by PCORI (with sessions conducted in 2015-2017).

The **USA Patient Network,** a 501(c)(3), consists of patients, caregivers, and their friends and family members that are united by a common goal: to make sure that medical treatments are as safe, effective, and as affordable as possible. Representing individuals from across the United States, we are educating ourselves and others about the **treatment standards** that are most important to us, including **improving quality of life**, and the **symptoms and health outcomes** that **matter most to patients**. A major aspect of our work is to provide patients' perspectives to federal agencies and medical and public

health researchers. Unlike most patient groups, the USA Patient Network **does not** accept funding from pharmaceutical or medical device companies, or insurance companies.

Included below is **a public version of my comment to the FDA on August 11, 2020**, designed to spread the word to a lay readership about IND stage communication issues at the FDA affecting everyday patients. I've written and included it as such with an understanding that the FDA may not be able to communicate about these issues as openly, given its current user fee structure based on PDUFA VI, and may additionally be limited by lack of congressionally allocated funding to date. However, as you will see, I join millions of other patients, caregivers, and clinicians across the country in my hope that the FDA will rise to the occasion to include grassroots patients' perspectives as a central, non-negotiable tenet of each phase of drug development and as integrated into its communication with industry sponsors. Currently, grassroots patients who are genuinely free of conflicts of interest are not only not "at the table" during FDA and industry communication, these patients are actually not even "in the room". Such exclusion is antithetical to the FDA's mission and promise.

Peer-reviewed articles I've hyperlinked throughout the comment submission are cited below.

In closing, **thank you for your time and consideration** as you work to improve communication at IND stages of drug development by acting upon many commenters' separate requests that the FDA include grassroots patients in advisory boards and working groups. Such measures would better ensure transparency in trial design and accountability to gold standard safety and efficacy measurements that are most meaningful to patients.

With gratitude to all FDA staff, and best wishes for a patient-accountable agency and pro-health economy,

Marie Garlock, PhD
Board Member, USA Patient Network
Community Leader for Change, Breast Cancer Action

Peer-reviewed article citations:

Abola, Matthew V, Prasad, Vinay. 2016. "Characteristics and Conflicts of Public Speakers at Meetings of the Oncologic Drugs Advisory Committee to the US Food and Drug Administration." *JAMA Internal Medicine*. 176(3):389–391. doi:10.1001/jamainternmed.2015.7805

Chen Emerson Y, Haslam Alyson, Prasad, Vinay. 2020. "FDA Acceptance of Surrogate End Points for Cancer Drug Approval: 1992-2019." *JAMA Internal Medicine.* 180(6):912–914. doi:10.1001/jamainternmed.2020.1097

Gyawali Bishal, Hey Spencer P, Kesselheim, Aaron, S. 2020. "Evaluating the evidence behind the surrogate measures included in the FDA's table of surrogate endpoints as supporting approval of cancer drugs." *EClinicalMedicine*. 21(100332). doi: 10.1016/j.eclinm.2020.100332

Institute of Medicine (US) Forum on Drug Discovery, Development, and Translation. 2007. "Chapter 2: Addressing the FDA's Resource Challenges." in Challenges for the FDA: The Future of Drug Safety, Workshop Summary. Washington (DC): National Academies Press (US). Retrieved August 31, 2020. (https://www.ncbi.nlm.nih.gov/books/NBK52926/)

Kesselheim, Aaron S., Woloshin, Steven, Eddings, Wesley, Franklin, Jessica M., Ross, Kathryn M. Schwartz, Lisa M. 2016. "Physicians' Knowledge About FDA Approval Standards and Perceptions of the 'Breakthrough Therapy' Designation." *JAMA*. 315(14):1516-1518. doi:10.1001/jama.2015.16984

Lex, Jon. 2016. "Why the Watchdog Won't Bite: U.S. Food and Drug Administration Challenges." *Western Journal of Emergency Medicine*. 17(6):747-748. doi:10.5811/westjem.2016.9.32492

Lietzan, Erika. 2020."FDA's Reliance on User Fees." Yale Journal on Regulation. Retrieved September 1, 2020. (https://www.yalejreg.com/nc/fdas-reliance-on-user-fees/)

National Cancer Institute. 2019. "Financial Toxicity and Cancer Treatment (PDQ®)–Health Professional Version." Retrieved August 22, 2020. (https://www.cancer.gov/about-cancer/managing-care/track-care-costs/financial-toxicity-hp-pdq).

Rupp, Tracy, Zuckerman, Diana. 2017. "Quality of Life, Overall Survival, and Costs of Cancer Drugs Approved Based on Surrogate Endpoints." *JAMA Internal Medicine.* 177(2):276-277. doi:10.1001/jamainternmed.2016.776

Schwartz, Lisa M, Woloshin, Steven. 2019. "Medical Marketing in the United States, 1997-2016." *JAMA.* 321(1):80-96. doi:10.1001/jama.2018.19320

Investigative journalism citations:

Perry, Susan. 2016. "New patient-advocacy group 'outed' by Minnesota-based website as 'Astroturf' campaign." Minneapolis Post. Retrieved August 31, 2020. (https://www.minnpost.com/second-opinion/2016/02/new-patient-advocacy-group-outed-minnesota-based-website-astroturf-campaign/)

Walker, Edward T. 2014. "What's the difference between political grassroots and big-interest Astroturf?". UCLA Newsroom. Retrieved September 3, 2020. (https://newsroom.ucla.edu/stories/whats-the-difference-between-political-grassroots-and-big-interest-astroturf)

FDA citations:

U.S. FDA Adverse Events Reporting System (FAERS). 2020. "Search: Gemzar, Gemcitabine, Gemcitabine/Hydrochloride, Gemcitabine/Oxaliplatin, Gemcitabine/Oxaliplatin/Rituximab." Retreived August 31, 2020. (https://fis.fda.gov/sense/app/d10be6bb-494e-4cd2-82e4-0135608ddc13/sheet/45beeb74-30ab-46be-8267-5756582633b4/state/analysis)

U.S. FDA. "Surrogate Endpoint Resources for Drug and Biologic Development." Retrieved August 31, 2020. (https://www.fda.gov/drugs/development-resources/surrogate-endpoint-resources-drug-and-biologic-development)