Global Headquarters
5005 LBJ Freeway, Suite 526
Dallas, Texas 75244
1-877 GO KOMEN | komen.org

December 7, 2020

VIA ELECTRONIC SUBMISSION

Stephan Hahn, M.D.
Commissioner
Food and Drug Administration
Dockets Management Staff (HFA-305),
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Premenopausal Women with Breast Cancer: Developing Drugs for Treatment Guidance for Industry Dockets Management Staff (HFA-305)

Dear Commissioner Hahn:

I am writing to you on behalf of Susan G. Komen (Komen) in response to the Food and Drug Administration's (FDA's) draft guidance, "Premenopausal Women with Breast Cancer: Developing Drugs for Treatment Guidance for Industry." Komen is the world's leading nonprofit breast cancer organization representing the millions of women and men who have been diagnosed with breast cancer. Komen has an unmatched, comprehensive 360-degree approach to fighting this disease across all fronts—we advocate for patients, drive research breakthroughs, improve access to high quality care, offer direct patient support and empower people with trustworthy information. Komen is committed to supporting those affected by breast cancer today, while tirelessly searching for tomorrow's cures. We advocate on behalf of the estimated 279,100 women and men in the United States who will be diagnosed with breast cancer and the more than 42,690 who will die from the disease in 2020 alone.

Comments on Draft Guidance

Komen appreciates the opportunity to provide comments for consideration on the FDA's recommendations regarding drug development and premenopausal women with breast cancer. Komen strongly affirms inclusion of younger, pre-menopausal women in drug development and clinical trials. Inclusion of premenopausal women in breast cancer product development programs will result in more complete information to inform clinical decision making and bring safe and effective therapies in a timely manner to this patient population.

It is currently estimated that about 18 percent of invasive breast cancers and about 11 percent of breast cancer deaths occur in women under 50 (pre-menopausal), killing approximately 4,600 women per year.[1] **Younger women diagnosed with breast cancer often have more aggressive disease or are diagnosed at a more advanced stage, making the timely availability of treatment options even more critical.**

[1] American Cancer Society's Breast Cancer Facts & Figures for 2019-2020

We believe that the basis on which premenopausal women have been excluded is flawed. Historically, premenopausal women have been excluded from clinical trials that investigated the efficacy of hormonal drugs for the treatment of hormone positive breast cancer, largely due to concerns about potential differences in how these hormonal drug and biological products would behave in premenopausal versus postmenopausal women. **This exclusion resulted in delays in availability of these therapies for premenopausal women.** Sufficient estrogen suppression can be employed, and as such, hormonal drug and biological products are likely to have similar efficacy and safety in premenopausal women as in postmenopausal women. Therefore, separate trials for this population is unnecessary.

Denying inclusion or delaying the availability of such therapies essentially deprives this group of patients potentially lifesaving treatment options. Premenopausal patients often are raising families and are participating in the workforce at high rates[2] – meaning that limited access to drugs and trials also may result in real, long-term societal and economic harm. **Any delays in treatment availability hurt patients, families, and the United States' workforce productivity.**

There are other strong considerations to support this inclusion, particularly in light of the current nationwide reckoning on health inequities. According to the same source referenced above, Black women under 40 have higher incidence rates of breast cancer than White women – i.e. more premenopausal Black women are getting breast cancer than premenopausal White women. Additionally, HR+/HER2- breast cancers are by far the most common subtype among women of all races/ethnicities. Non-Hispanic, Black women are diagnosed with the HR+/HER2- cancer subtype at a rate of about 21 percent, which is about double the proportion of this subtype in other racial and ethnic groups.[3] The higher breast cancer death rate in Black women is also in part a reflection of the disproportionate burden of triple negative breast cancers in this group.[4] **Thus, including premenopausal women in drug development trials also may increase clinical trial diversity and improve outcomes for Black breast cancer patients and survivors.**

However, we must note that this policy alone is not a "silver bullet" to increasing clinical trial diversity as clinical trials are by their nature exclusionary. For example, if clinical trials continue to exclude participants based on other criteria which disproportionately impact marginalized communities or fail to address the financial burden clinical trials place on participants, progress in health equity may be delayed. **As such, enrollment of premenopausal women must reflect the diversity of patients diagnosed at younger ages and accommodate these issues.**

While clinical research should not use menopausal status as an exclusion factor, we support FDA's suggestion that menopausal status should be captured. Moreover, we suggest that **the type and duration of estrogen suppression therapy which patients are receiving should also be captured** as this may have an impact on outcomes or side effects which can dramatically change quality of life on a given therapy. Additionally, Komen suggests that the FDA provide more clarity, based on the agency's review of the nonclinical, clinical pharmacology and clinical literature, of which constitutes "adequate estrogen suppression" as this may assist industry approaches to clinical study design.

---

[2] U.S. Bureau of Labor Statistics women under 50 are employed at a rate of 72%. Of all women with children under 18 years of age, 71.4% are employed. Among mothers with children 6 to 17 years old, 76.5%, are employed which is higher than for those with younger children. The rate for those with children under 6 years old was 64.7 %, and the rate for women with children under 3 years old was 62.0 %. Unmarried mothers are more likely to participate in the labor force than married mothers as 77.3%, compared with 69.0% of married mothers.

[3] American Cancer Society's Breast Cancer Facts & Figures for 2019-2020

[4] *Id.*

As highlighted by the guidance document, collecting information on the long-term clinical effects of cancer treatment is especially important for younger, premenopausal women, as this may impact quality of life throughout their cancer journeys. However, **Komen suggests that the FDA go further and add long-term follow-up (beyond five years), post-market/confirmatory studies, and real-world evidence to supplement the data and more fully understand the long-term effects of cancer treatment.**

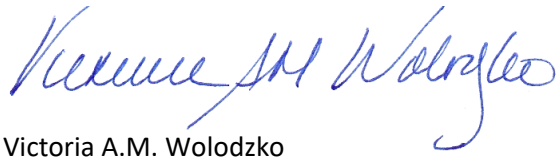
Finally, Komen applauds consideration of the potential effects of cancer drugs on fertility, as this is of particular interest to many premenopausal women as this information could allow them to make informed decisions about treatment options, including fertility preservation. Komen appreciates that fertility and fertility preservation are largely outside the scope of this Draft Guidance, however these areas are incredibly important for young breast cancer patients. As such, **Komen strongly encourages FDA to provide further guidance or develop a request for information on fertility and fertility preservation for cancer patients.**

Conclusion

Komen thanks the FDA for the opportunity to provide comments. We share the goal to ensure the best possible outcomes for breast cancer patients and survivors today and in the future. We reiterate our strong support for inclusion of younger, pre-menopausal women in drug development and clinical trials, which we believe will result in more complete information to inform clinical decision making and bring safe and effective therapies in a timely manner to this patient population.

If you have any questions, or we may be of further assistance, please do not hesitate to reach out to Molly Guthrie, Director of Public Policy and Advocacy, at mguthrie@komen.org.

Sincerely,



Victoria A.M. Wolodzko
Senior Vice President, Mission
Susan G. Komen