Docket No. FDA-2024-N-3528 for "Advancing Rare Disease Therapies Through an FDA Rare Disease Innovation Hub; Public Meeting; Request for Comments."

October 30, 2024

Dear FDA Officials,

On behalf of The LAM Foundation, I would like to express our strong support for the establishment of the FDA Rare Disease Innovation Hub. As an organization dedicated to finding safe and effective treatments and ultimately a cure for lymphangioleiomyomatosis (LAM)—a rare lung disease that primarily affects women—we are proud that LAM is one of the few rare diseases with an FDA-approved treatment.[1] While this breakthrough has provided hope for our patient community, there remains an urgent need for further research, alternate therapies, and patient support. The creation of the Innovation Hub represents a crucial opportunity to build on such successes and address the ongoing challenges rare disease patients face in drug development.

We offer the following recommendations to ensure that the Rare Disease Innovation Hub maximizes its impact for patients, especially those affected by rare diseases that disproportionately impact women:

1. **Prioritizing Women's Health in Rare Disease Research**:
   Rare diseases like LAM, which predominantly affect women, often face significant research and funding gaps. As such, we urge the FDA to ensure that the Innovation Hub specifically prioritizes rare diseases that disproportionately affect women. This focus will help address longstanding gender disparities in health research, promoting greater equity in developing life-saving treatments for women with rare conditions and enhancing their quality of life.

2. **Patient-Centered Collaboration**:
   The LAM Foundation has long championed the inclusion of patients as essential partners in the research process. LAM patients have a strong history of participating in clinical trials, engaging in the creation of patient registries and databases, and contributing to the

[1] McCormack FX, Inoue Y, Moss J, et al. Efficacy and safety of sirolimus in lymphangioleiomyomatosis. *N Engl J Med*. 2011;364(17):1595-1606.

design of studies that reflect their lived experiences. We recommend that the FDA formalize avenues within the Hub to involve patients early and throughout the development and review of rare disease therapies. Their insights, particularly from women living with chronic rare diseases like LAM, are invaluable in shaping meaningful outcomes.

3. **Enhancing Diagnosis and Treatment through Biomarkers:**
   Biomarkers are essential in advancing women's health in rare disease, where they play a critical role in improving diagnosis, monitoring, and outcomes, with proven applicability in LAM.[2] For women with rare diseases, biomarkers provide crucial insights into disease progression and treatment response, often making it possible to identify conditions earlier and monitor them more effectively. This has specific importance given that rare diseases may present differently in women and often lack sex-specific data. By investing in biomarker research and development, the FDA can help foster more tailored treatments, ensuring that women with rare diseases receive more accurate diagnoses and effective care.

4. **Innovative Clinical Trial Designs for Small Populations**:
   As LAM is a rare disease with a small patient population, traditional clinical trial models are often impractical. We encourage the FDA to leverage adaptive trial designs, real-world evidence, n=1, and decentralized trials within the Innovation Hub to streamline clinical development for rare diseases. Flexibility in trial design will not only expedite access to therapies but also reduce the burden on patients, many of whom are women juggling unique health and caregiving responsibilities.

5. **Expansion of the Accelerated Approval Pathway for Rare Disease Therapies**:
   The LAM Foundation supports the expanded use of the Accelerated Approval Pathway for rare diseases, particularly where no approved treatments exist. For conditions like LAM, where women often wait years for a correct diagnosis, rapid access to therapies is critical. We encourage the FDA to apply this pathway more broadly within the Rare Disease Innovation Hub, ensuring that innovative treatments for women's health are given priority consideration.

[2] Young L, Lee HS, Inoue Y, et al. Serum VEGF-D a concentration as a biomarker of lymphangioleiomyomatosis severity and treatment response: a prospective analysis of the Multicenter International Lymphangioleiomyomatosis Efficacy of Sirolimus (MILES) trial. *Lancet Respir Med*. 2013;1(6):445-452.

6. **Global Collaboration for Rare Disease Research**:
   Given that LAM affects women worldwide, we strongly support efforts to enhance international regulatory collaboration. The LAM Foundation actively partners with global collaborators in research, clinical expertise, and advocacy, and we believe that harmonizing regulatory frameworks across borders will accelerate the development of treatments for rare diseases affecting women around the world.

We are grateful for the FDA's leadership in establishing the Rare Disease Innovation Hub. We look forward to ongoing engagement to ensure that women's health in rare diseases remains at the forefront of this critical initiative. The LAM Foundation remains committed to advocating for the unique needs of women with LAM and contributing to the success of the Hub. Thank you for considering our comments.

Sincerely,

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