December 17, 2025

Martin A Makary, MD, MPH
Commissioner
U.S. Food and Drug Administration
White Oak Campus
10903 New Hampshire Avenue
Silver Spring, MD 20993

Via e-mail: commissioner@fda.hhs.gov

Dear Commissioner Makary:

On behalf of the American Society of Transplant Surgeons (ASTS) and American Society of Transplantation (AST), we are deeply grateful for the Trump Administration's previous efforts to increase access to transplantation and for its strong interest in advancing the field, evidenced most recently at the September 18, 2025, press event with respect to xenotransplantation.

There is another issue of great concern where your help would be transformative – addressing stagnation in kidney transplant immunosuppressive drug development.
This stagnation in drug development is mainly attributable to the clinical trial endpoint used by the FDA to evaluate new drugs in this product category. The solution is clear – FDA qualification of the Composite Biomarker Panel (iBox) as a reasonably likely surrogate co-primary endpoint for use in the accelerated approval pathway. Such approval has the potential to trigger development of a new generation of immunosuppressive drugs that may not only extend the lives and improve the quality of life of the country's growing population of kidney transplant recipients but also help alleviate the demand for this scare resource.

The unmet need for new immunosuppressive drugs in kidney transplantation is clinically documented and indisputable.

- The last novel agent approved for prophylaxis of organ rejection in adult patients receiving a kidney transplant occurred almost 15 years ago.
- While renal allograft survival one year post transplant exceeds 93%[i], long term renal allograft survival has not improved significantly over the past two decades.
- Over the past eight years, the FDA sponsored four public meetings on the future of transplant drug innovation and unmet patient needs. Transplant[ii] and patient advocacy organizations – including the largest independent kidney patient advocacy organization in the country (the American Association of Kidney Patients[iii]) – consistently emphasized the pressing need for the agency to accelerate approval of new immunosuppressants and to focus on long term graft and patient survival (beyond one year).

The FDA's current clinical trial endpoint for the approval of new immunosuppressive drugs for renal transplant recipients must be modernized.
The current endpoint is a composite endpoint of death, graft loss, and acute rejection assessed at one-year post-transplant. The challenges posed by this endpoint are threefold:

1) The current endpoint erects a high barrier for potential sponsors of new immunosuppressive drugs to demonstrate superiority given the efficacy of already-approved kidney transplant immunosuppressive drugs at one-year post-transplant and,
2) There is little or no incentive for sponsors to invest in the development of new immunosuppressive drugs when those drugs are substantially equivalent (non-inferior) to established and readily available immunosuppressive drugs and,
3) The current endpoint is poorly prognostic and not predictive of long-term graft survival.

The Transplant Therapeutics Consortium (TTC), a public-private partnership, provides the answer.

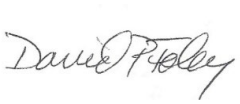
The TTC, established by ASTS and AST in 2017, was founded to work with the FDA to develop a Drug Development Tool for use as a surrogate endpoint for clinical trials for new immunosuppressive drugs to be used in the setting of kidney transplantation. The resulting reasonably likely surrogate endpoint – iBox – is a Composite Biomarker Panel that utilizes an artificial intelligence-based algorithm to predict long term renal graft survival. The iBox is the result of over six years of work by a team of experts in the field, which culminated in the submission of the Full Qualification Package (FQP) in February 2025.

This Composite Biomarker Panel (iBox) was initially accepted into the FDA Biomarker Qualification Program in the Letter of Intent as a substitute for FDA's current endpoint, but the FDA's Division of Rheumatology and Transplant Medicine (DRTM) subsequently indicated that the current endpoint must continue to be used, therefore the Composite Biomarker Panel would be at best, a co-primary endpoint. Even if the Composite Biomarker Panel is qualified as a reasonably likely surrogate endpoint, a new immunosuppressive drug would still be required to meet the current endpoint, but the drug sponsor would have the option to market superiority if the Composite Biomarker Panel endpoint were met. ASTS and AST are confident that qualification of the Composite Biomarker Panel as a co-primary endpoint for use in the accelerated approval pathway would increase interest in the development of new immunosuppressive drugs to extend the graft and patient survival of kidney transplant recipients.

Given the widespread clinical consensus developed through the TTC public-private partnership and the pressing need for innovation in this area, we ask that your office take an active role in reviewing the upcoming FDA Qualification Recommendation (expected in the spring on 2026) and arrange a meeting with the TTC to ensure that all the facts are considered in making this determination. As the two largest transplantation societies in the United States, representing over 7,400 experts dedicated to transplantation, it is vitally important that we meet with you, at your earliest convenience to ensure that this innovative strategy is employed by the FDA for the patients we serve. ASTS Associate Director, Advocacy & Professional Practices, Emily Besser (Emily.besser@asts.org), will be contacting your team to schedule a meeting.

Respectfully,

James F. Markmann, MD, PhD
President, ASTS



David P. Foley, MD
President, AST

[i] https://usrds-adr.niddk.nih.gov/2024/end-stage-renal-disease/7-kidney-transplant
[ii] https://www.amjtransplant.org/article/S1600-6135(25)02860-6/fulltext
[iii] https://aakp.org/wp-content/uploads/2023/10/Future-of-Transplant-Drug-Innovation_Survey-Slides_FINAL-10.12.23.pdf