



April 28, 2026

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:

We are writing today as current and former Presidents of the American Society of Transplantation (AST) and the American Society of Transplant Surgeons (ASTS) to urge you to hold a roundtable meeting on strategies to address the urgent need to accelerate the development and approval of new immunosuppressive therapies for transplant recipients. Specifically, we urge a focus on the need to qualify the Composite Biomarker Panel (iBox) as a reasonably likely surrogate endpoint (RLSE) for kidney transplant clinical trials under the Accelerated Approval pathway.

We believe that a thorough review of iBox, including hearing directly from experts and stakeholders, ultimately will lead to FDA support and qualification of the iBox as a co-primary endpoint and as a RLSE. The iBox is an AI-derived biomarker that is prognostic and predictive of long-term (five year) kidney transplant graft survival. The accuracy of the iBox in predicting graft survival has been tested in four validation sets, two of which are randomized controlled trials. The qualification of the iBox was led by the Transplant Therapeutics Consortium (TTAC), a public private partnership with the FDA, AST and ASTS. A RLSE qualification would provide biopharmaceutical companies an accelerated approval pathway to demonstrate superiority over conventional (old) immunosuppressive drugs, spurring much-needed investment of resources in this area.

We appreciate your commitment to streamlining administrative processes and facilitating innovation in new drug development. While there has been important progress in transplantation, meaningful improvements in long-term post-transplant outcomes have lagged behind. There is a pressing and growing need for innovation in the development of new immunosuppressive drugs. Transplant recipients are suffering from the significant side effects of current immunosuppressive medications, and new medications are desperately needed that improve long term graft survival and decrease side effects. These impactful side effects from existing FDA-approved immunosuppressives result in many patients skipping doses, thus putting their organs at risk of failure. However, for new medications to be developed, industry needs an expedited pathway to approval and a means to demonstrate benefit (superiority) over current standard of care regimens from the 1990's.

Qualifying iBox would represent an important step forward for clinical research in transplantation and help expand access to innovative therapies for transplant recipients. If qualified, it would give drug sponsors a pathway to pursue accelerated approval of novel agents that demonstrate superiority over current



immunosuppressive therapies and have the potential to improve the long-term survival of transplanted kidneys.

Significantly, the iBox as a co-primary endpoint would not pose any risk to patient safety: If iBox were qualified as a co-primary endpoint, a pharmaceutical company seeking approval of a new immunosuppressive drug still would be required to demonstrate safety using the same standards currently in place including the assessment of death post-transplant; however, to demonstrate effectiveness for accelerated approval, the company would have to demonstrate **not only** that the new drug results in one-year acute rejection that is at least noninferior to that of drugs currently on the market (the current effectiveness standard) **but also** that the new drug's iBox score (a predictor of long term graft survival) is superior to the standard of care. Approval of the iBox score as a co-primary endpoint poses no risk to patient safety or to the reputational integrity of the FDA review process.

* * * * *

It is critical that we modernize the approval process to provide transplant recipients with more treatment options that could reduce post-transplant complications and extend the lifespan of the transplanted organ. Our patients deserve nothing less.


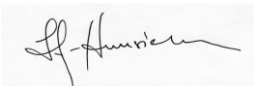

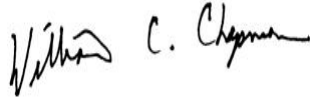







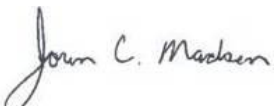
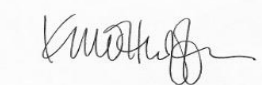
Given our leadership roles within our institutions and across the transplant community -- and the urgency of this issue -- we are taking the unprecedented step of joining together to urge the FDA to convene a roundtable with leading kidney transplant experts to discuss these important issues. This discussion should focus on the significant unmet needs of patients, the strong clinical consensus supporting iBox, and the importance of encouraging greater investment in the development of new transplant therapies. We would be happy to work with you to support this effort.

Sincerely,



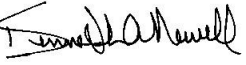
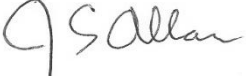
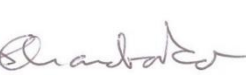





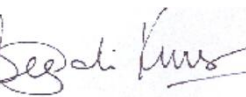
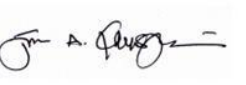
David Foley, MD
AST President

James Markman, MD
ASTS President

Nicole Turgeon, MD, FACS
AST President-Elect

Robert B. Ettenger, MD (1984–1985) Institution: University of California, Los Angeles	<i>Email confirmation</i> 4/24/2026	Ginny Bumgardner, MD, PhD (2024 – 2025) The Ohio State University	
Lawrence G. Hunsicker, MD (1987–1988) Institution: University of Iowa		Elizabeth Pomfret, MD, PhD (2023 – 2024) University of Colorado	
Ronald H. Kerman, PhD (1991–1992) Institution: Baylor College of Medicine	<i>Email confirmation</i> 4/24/2026	William Chapman, MD (2022 – 2023) Washington University School of Medicine, St. Louis	
Manikkam Suthanthiran, MD (1993–1994) Institution: NY Presbyterian Hospital	<i>Email confirmation</i> 4/24/2026	A. Osama Gaber, MD (2021 – 2022) Houston Methodist	
Thomas A. Gonwa, MD (1994–1995) Douglas J. Norman, MD (1995–1996) Institution: Oregon Health & Science University	<i>Email confirmation</i> 4/24/2026	Marwan Abouljoud, MD, MBA (2020 – 2021) Henry Ford Hospital	
J. Harold Helderman, MD (1997–1998) Institution: Vanderbilt University Medical Center	<i>Email confirmation</i> 4/24/2026	Lloyd Ratner, MD, MPH (2019 – 2020) Columbia University	
John F. Neylan, MD (1998–1999) Institution: Angion Biomedica Corporation	<i>Email confirmation</i> 4/25/2026	Dixon Kaufman, MD, PhD (2018 – 2019) University of Wisconsin	<i>Email confirmation</i> 4/26/2026 8:34 AM ET
John R. Lake, MD (1999–2000) Institution: University of Minnesota	<i>Email confirmation</i> 4/24/2026	Jean Emond, MD (2017 – 2018) Columbia University	<i>Email confirmation</i> 4/28/2026 10:51 AM ET
Mohamed H. Sayegh, MD (2000–2001) Institution: American University of Beirut		Timothy Pruett, MD (2016 – 2017) University of Minnesota	<i>Email confirmation</i> 4/24/2026 5:13 PM ET
Laurence A. Turka, MD (2001–2002) Institution: Massachusetts General Hospital	<i>Email confirmation</i> 4/24/2026	Charles Miller, MD (2015 – 2016) The Cleveland Clinic	
Jay Alan Fishman, MD (2004–2005) Institution: Harvard Medical School	<i>Email confirmation</i> 4/24/2026	Peter Stock, MD, PhD (2014 – 2015) University of California, San Francisco	
Jeffrey S. Crippin, MD (2006–2007) Institution: Washington University School of Medicine, St. Lois		Alan Langnas, DO (2013 – 2014) University of Nebraska Medical Center	<i>Email confirmation</i> 4/27/2026 4:25 PM ET
Joren C. Madsen, MD, DPhil (2009–2010) Institution: Massachusetts General Hospital Transplant Center		Kim Olthoff, MD (2012 – 2013) University of Pennsylvania	
Maryl Johnson, MD	<i>Email confirmation</i>		



(2010–2011)	4/24/2026	
Institution: University of Wisconsin		
Robert S. Gaston, MD		John Roberts, MD (2008 – 2009) University of California, San Francisco <i>Email confirmation</i> 4/24/2026 4:22 PM ET
(2011–2012)		
Institution: University of Alabama at Birmingham		
Roslyn B. Mannon, MD		Goran Klintmalm, MD, PhD (2007 – 2008) Baylor University Medical Center <i>Email confirmation</i> 4/27/2026 8:08 PM ET
(2012–2013)		
Institution: University of Nebraska Medical Center		
Kenneth A. Newell, MD, PhD		Richard Howard, MD, PhD (2004 – 2005) <i>Email confirmation</i> 4/27/2026 5:38 PM ET
(2014–2015)		
Institution: Emory University School of Medicine		
James S. Allan, MD, MBA		Abraham Shaked, MD (2003 – 2004) University of Pennsylvania <i>Email confirmation</i> 4/27/2026 3:49 PM ET
(2015–2016)		
Institution: Massachusetts General Hospital		
Anil Chandraker, MD, FASN,		James Schulak, MD (2002 - 2003) <i>Email confirmation</i> 4/25/2026 8:05 PM ET
FAST, FRCP		
(2016–2017)		
Institution: University of Massachusetts		
Ronald G. Gill, PhD		Nancy Ascher, MD, PhD (2000 -2001) University of California, San Francisco <i>Email confirmation</i> 4/24/2026 5:28 PM ET
(2017–2018)		
Institution: University of Colorado		
Dianne McKay, MD, FAST		Ronald Busuttil, MD, PhD (1999 – 2000) University of California, Los Angeles <i>Email confirmation</i> 4/27/2026 8:08 PM ET
(2018–2019)		
Institution: Scripps Research		
Emily Blumberg, MD, FAST		Mark Hardy, MD (1994 – 1995) Columbia University <i>Email confirmation</i> 4/27/2026 8:53 PM ET
(2019–2020)		
Institution: Hospital of the University of Pennsylvania		
Richard Formica, Jr., MD, FAST		
(2020–2021)		
Institution: Yale University School of Medicine		
John Gill, MD, MS, FAST		
(2021–2022)		
Institution: University of British Columbia		
Deepali Kumar, MD, MSc,		
FRCPC, FAST (2022–2023)		
Institution: University Health Network Toronto		
Jon Kobashigawa, MD		
(2024–2025)		
Institution: Cedars-Sinai Smidt Heart Institute		