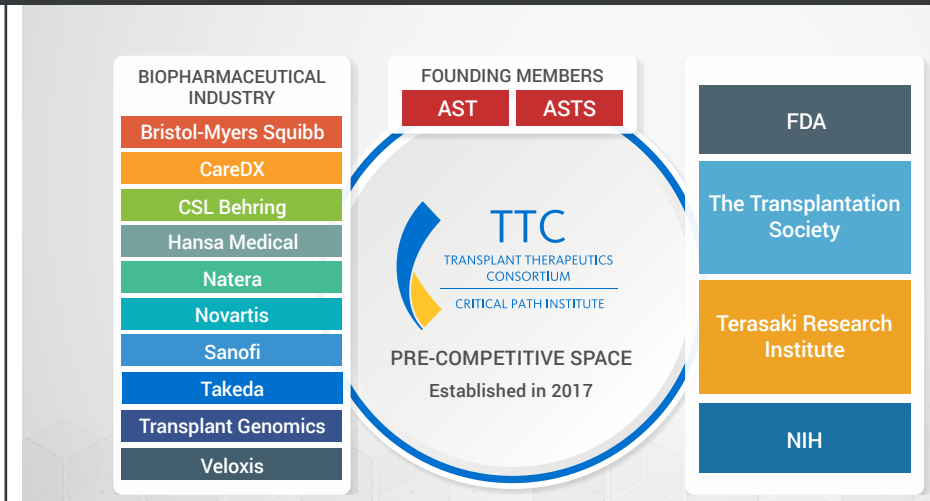
CRITICAL PATH INSTITUTE

TRANSPLANT THERAPEUTICS CONSORTIUM IMPACT ON DRUG DEVELOPMENT

Critical Path Institute's Transplant Therapeutics Consortium

- Public-private partnership of diverse stakeholders across the transplant field and regulatory agencies
- Mission to accelerate the pace of drug development in the field of transplantation
- Pre-competitive engagement facilitates alignment of transplant field and regulatory authorities to identify challenges, prioritize solutions, and develop tools that usher new product development to meet the most pressing needs of transplant recipients



Collaboration to advance the drug development process facilitates individual successes advancing drug programs

Unmet Needs in Kidney Transplantation Care

- 10-year all cause kidney allograft failure is between 34 and 50%[1]
- Significant negative outcomes associated with graft failure, including return to dialysis, decreased quality of life, re-transplantation, and increased mortality
- Graft survival is the most important outcome to people living with a kidney transplant[2]

Challenges in IST Drug Development for Kidney Transplantation

- No acceptable surrogate or reasonably likely surrogate endpoint to open accelerated approval pathways
- Clinical trials must be large, lengthy, or rely on non-inferior design to show differentiation from the current standard of care IST regimens
- High cost of clinical trials and small patient population bring concerns of low return on investment

MOVING THE FIELD FORWARD TOWARDS DRUG DEVELOPMENT SOLUTIONS

SURROGATE ENDPOINT

Seeking endorsement of the iBox Scoring System as a reasonably likely surrogate endpoint with FDA and EMA to enable **accelerated approval** and **conditional marketing authorization pathways**

- The iBox Scoring System was developed and validated by the Paris Transplant Group to predict the probability of long-term kidney graft survival
- Developed using prospective cohort of 4,000 patients and validated in >3,500 patients from the US and Europe and in three clinical trials[3]
- Highly reliable in variety of patient populations and treatment settings

U.S. Food and Drug Administration

*Anticipate Qualification in Q1 2023**

- March 2019: Critical Path Innovation Meeting with FDA to discuss goals of the TTC and the iBox Scoring System. FDA encouraged individual drug sponsor conversations regarding use of iBox to open accelerated approval pathway, recommended seeking qualification as a reasonably likely surrogate endpoint
- June 2020: iBox Scoring System formally accepted into Biomarker Qualification Program with positive review of Letter of Intent Submission

European Medicines Agency

*Anticipate Qualification in Q1 2022**

- February 2020: Began informal discussion on Qualification of iBox scoring system through the Qualification of Novel Methodologies for Drug Development
- Q2 2021: Anticipated submission of Letter of Intent/Briefing Document to EMA

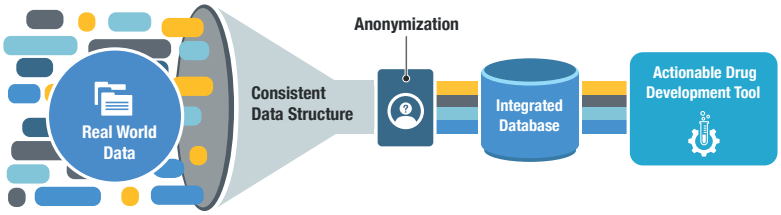
*Dates are dependent on the availability of data

DATA COLLABORATION

Standardization and integration of key patient-level data from individual clinical trials and real-world datasets to create an **aggregated database** to support regulatory endorsement submissions

FOSTERING INNOVATION

The TTC enables **pre-competitive collaboration** with industry, regulatory agencies, academia, and transplant societies to ensure wide-spread **consensus-based science** with all stakeholders



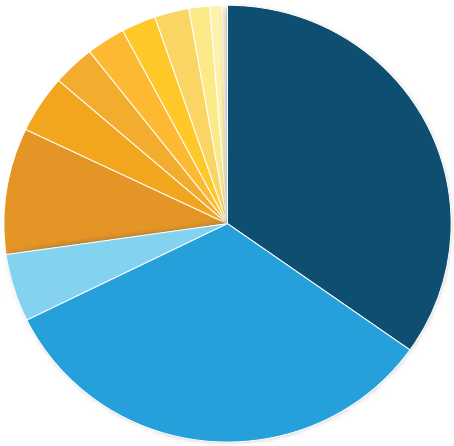
Globally Contributed Data

DATA TYPE:

- **19** Clinical Transplant Centers (n = 15,838)
- **10** Clinical Trial Datasets (n = 5,936)

DATA SOURCES:

- Europe (n = 7,580)
- North America (n = 7,165)
- South America (n = 1,093)



- Novartis: TRANSFORM (n = 2,037)
- Novartis: ELEVATE (n = 932)
- BMS: BENEFIT (n = 666)
- Novartis: US-92 (n = 613)
- BMS: BENEFIT-EXT (n = 543)
- Veloxis: LCP-3002 (n = 543)
- Veloxis: LCP-3001 (n = 326)
- CERTITEM (n = 194)
- BORTEJECT (n = 44)
- RITUX ERAH (n = 38)

Data acquired by TTC, as of January 2021

2018 SUCCESSES

- Whitepaper titled "The importance of drug safety and tolerability in the development of new immunosuppressive therapy for transplant recipients: The Transplant Therapeutics Consortium's position statement" published in *American Journal of Transplantation (AJT)* [4]
- TTC/FDA Co-hosted workshop titled "Evidence-Based Treatment Decision in Transplantation: The Right Dose & Regimen for the Right Patient/ Individualized Treatment" at FDA White Oak Campus in Silver Spring, MD
- Awarded Aim 1 of FDA BAA contract to support the development of quantitative drug development tools to optimize kidney transplant trial designs ($596,688 over 3 years)

2019 SUCCESSES

- FDA touts TTC efforts in an editorial titled "Public-private partnerships in transplant drug development" published in *AJT* [5]
- Awarded Aim 2 of FDA BAA contract to continue developing quantitative drug development tools ($998,184 over 2 years)

2020 SUCCESSES

- Meeting report titled "Use of biomarkers to improve immunosuppressive drug development and outcomes in renal organ transplantation" published in *AJT* [6]

We look forward to your support in making a meaningful and positive impact on transplant drug development and the lives of transplant recipients worldwide!

References

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4. Stegall MD et al. The importance of drug safety and tolerability in the development of new immunosuppressive therapy for transplant recipients: The Transplant Therapeutics Consortium's position statement. *Am J Transplant*. 2019 Mar;19(3):625-632. doi: 10.1111/ajt.15214. Epub 2019 Jan 23.
5. Albrecht R et al. Public-private partnerships in transplant drug development. *Am J Transplant*. 2020 Feb;20(2):377-381. doi: 10.1111/ajt.15604. Epub 2019 Oct 30.
6. Mannon RB et al. Use of biomarkers to improve immunosuppressive drug development and outcomes in renal organ transplantation: A meeting report. *Am J Transplant*. 2020 Feb 24.

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