Novel AAV Gene Therapy Treatment for ADPKD

Amy Rhoden Smith, Ph.D.
ASGCT Annual Conference
May 12, 2026

Disclosures

Amy Rhoden Smith is an employee and shareholder of Torque Bio.
Research funding for this work was provided by Torque Bio.

Unlocking the Next Era of Kidney Therapeutics

Founded in 2022

Backed by leading life science investors – Westlake Village BioPartners, Northpond Ventures, and Hatteras Ventures

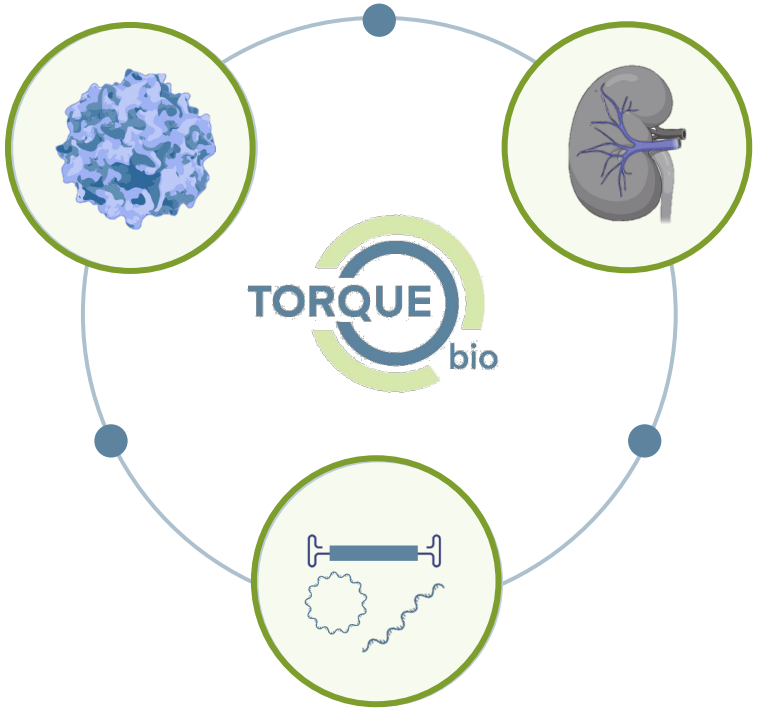
Technology

Built on exclusively licensed IP developed in Aravind Asokan's lab at Duke University and UNC

Therapeutic Focus

Developing AAV gene therapies targeting ADPKD, a leading genetic cause of kidney failure

A Differentiated Approach to Address ADPKD and Beyond



Novel, Kidney-Optimized Capsids

Enhanced, translatable renal tubule transduction

Localized Delivery Method

Direct kidney delivery minimizes systemic exposure and supports lower doses

Fit-for-Purpose Cargo

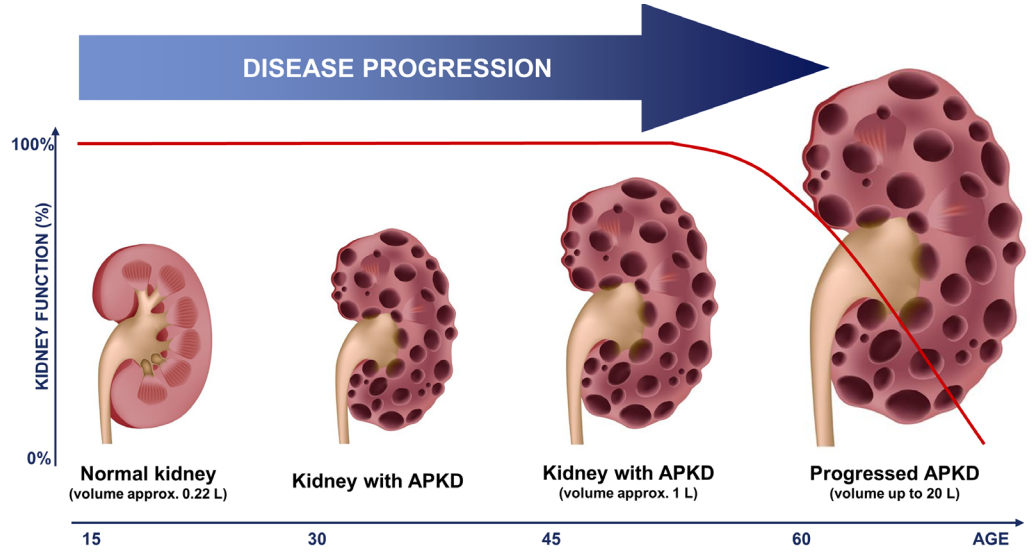
AAV-encoded circular RNAs and gene replacement strategies to target wide range of disorders

Our platform gives us the unique ability to address significant genetic diseases with high unmet need

Understanding Autosomal Dominant Polycystic Kidney Disease (ADPKD)

Progressive Genetic Disease Leading to Kidney Failure with No Curative Therapy

PKD1 or *PKD2* genetic mutations drive disease progression[1,2]



Mutations disrupt cell function and fluid regulation leading to continuous cyst growth and kidney decline

Prevalence: ~600,000 in US alone

Disease Progression:

- Symptom onset at 30-40 years
- Age of ESRD onset at >50 years*
- At ESRD, treatment options are dialysis or kidney transplant

Approved Treatments: Jynarque® slows progression, but doesn't address genetic root cause

Unmet Need: No curative options leads to inevitable kidney decline with high morbidity, lifelong-costs, and heavy emotional burden

[1]*Cloutier et al. 2020. BMC Health Serv Res. 2020*
[2]*Shonauer et al. Genetic Med. 2020.*
**Age of end-stage renal disease (ESRD) onset ~50 years (ADPKD1) and ~late 60s (ADPKD2)*

Torque's Lead Program is TQB-001 for Treating ADPKD2

RATIONALE

Loss of PC2 expression drives cystic phenotype in kidney tubule cells. Restoring PC2 expression can halt or even reverse cystogenesis.

STRATEGY

AAV-mediated *PKD2* gene replacement delivered directly to the kidney to increase PC2 expression.

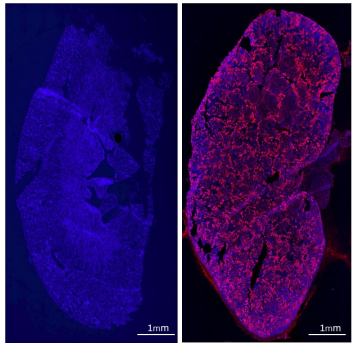
PC2; polycystin-2 protein

TQB-001 Development Candidate Utilizes Proprietary Kidney Capsid

AAVk.20 Kidney-Optimized Capsid

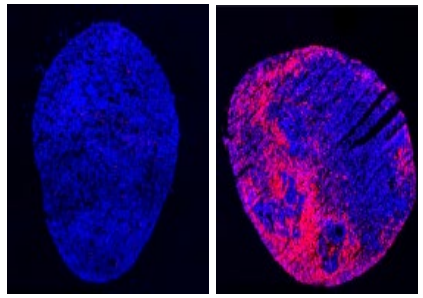
The AAVk.20 capsid was developed in Aravind Asokan's lab through cross-species evolution[1] and shows enhanced kidney transduction compared to AAV9:

Mouse Kidney



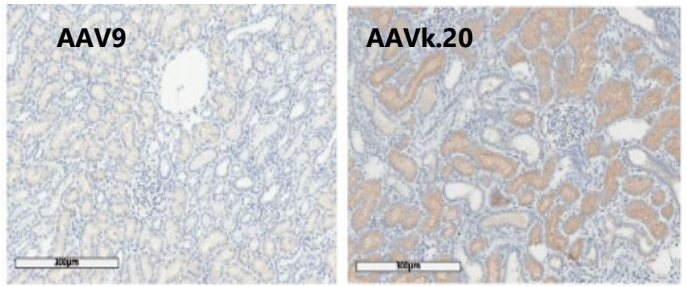
AAV9 AAVk.20

Human Kidney Organoid

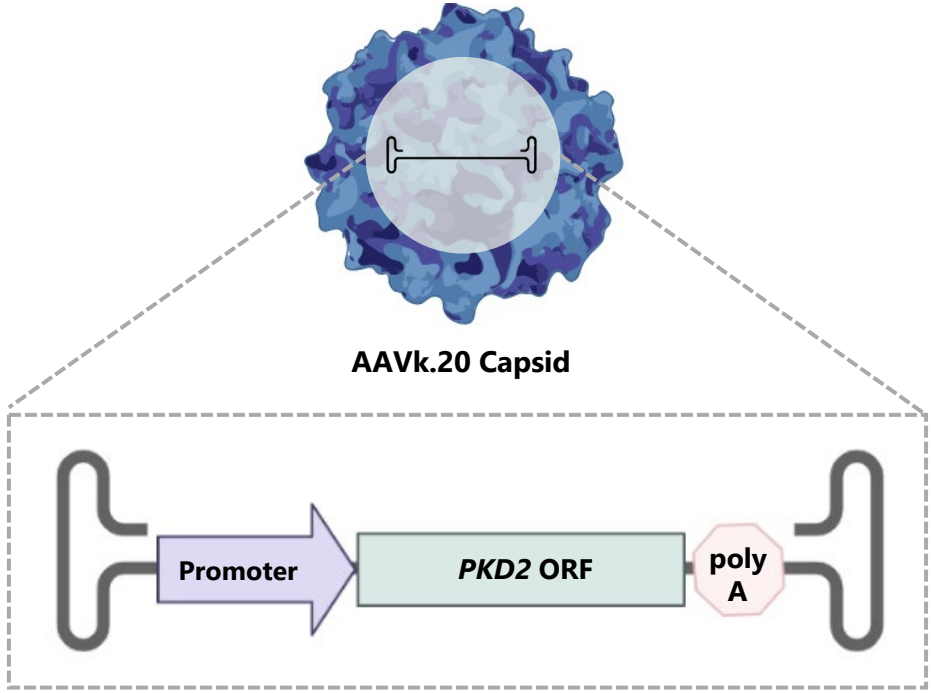


AAV9 AAVk.20

Pig Kidney



TQB-001 Vector

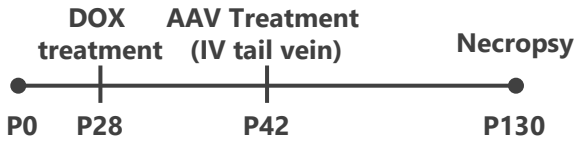


TQB-001 development candidate selection was made based on a data package encompassing in vitro expression, in vivo expression, and in vivo PoC activity

[1]Rosales et al. 2024. Nat Biomed Engin.
Kidneys (Mouse, Pig, NHP) and kidney organoids (Human) were transduced with AAVk.20 encoding an mCherry transgene

TQB-001 Reduces Cyst Burden in ADPKD2 Mice

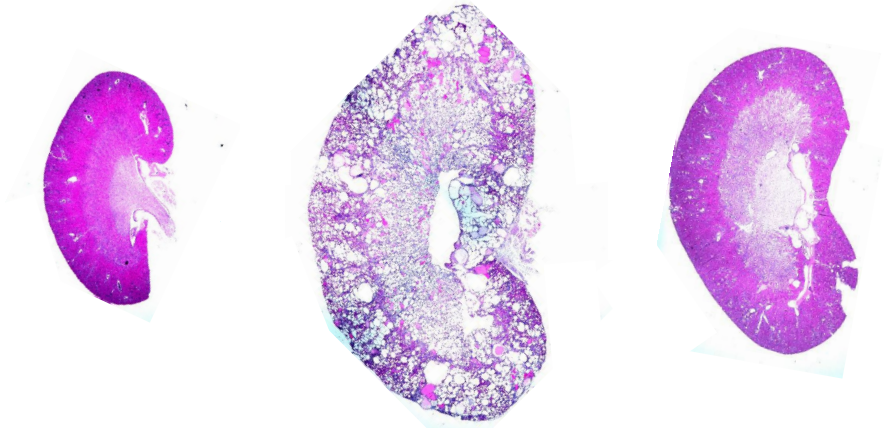
In Vivo PoC Study Design and Results
Doxycycline-inducible PKD2 KO Model



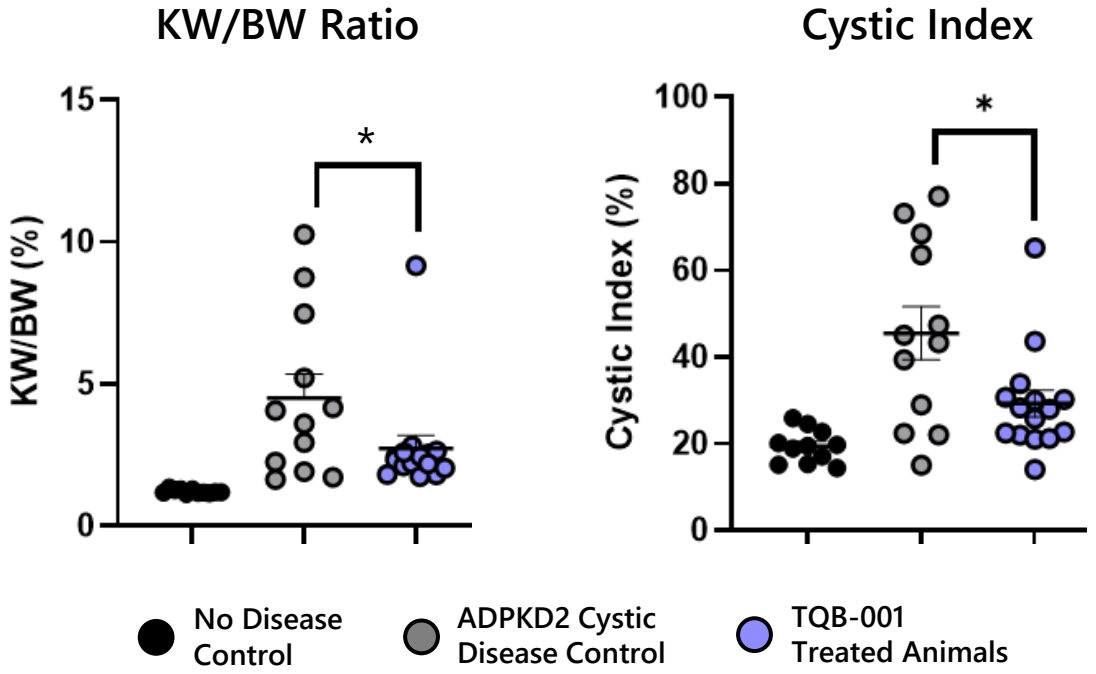
No Disease Control

ADPKD2 Cystic Disease Control

TQB-001 Treated Animal



Cystic Kidney Phenotype Assays

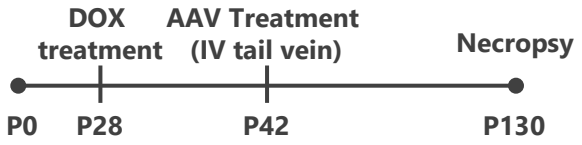


TQB-001 reduces cystic phenotype by >35%

Pkd2$^{fl/fl}$, Pax8-rtTA$^{+/}$, TetO-Cre$^{+/}$ mouse model, where doxycycline treatment knocks out PC2 expression specifically in kidney tubules by excising exons 11-13 in Pkd2 gene.
Representative H&E kidney images from each group, 1x magnification.
Treatment was performed with an HA-tagged version of TQB-001

TQB-001 Prevents Kidney Function Loss in ADPKD2 Mice

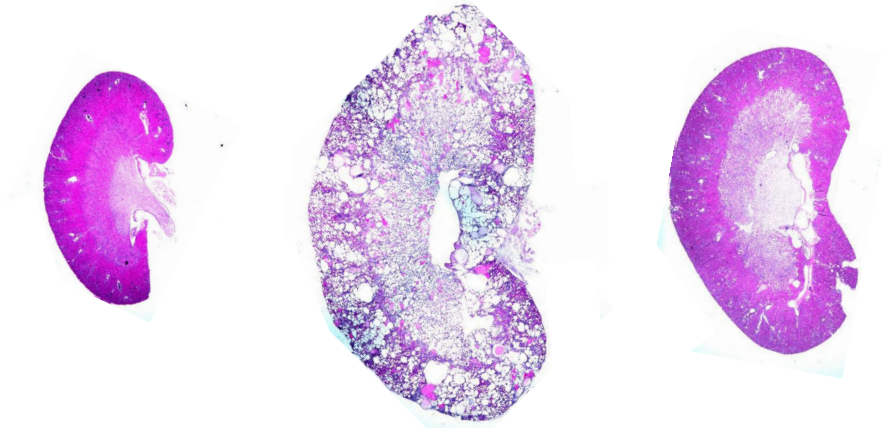
In Vivo PoC Study Design and Results
Doxycycline-inducible PKD2 KO Model



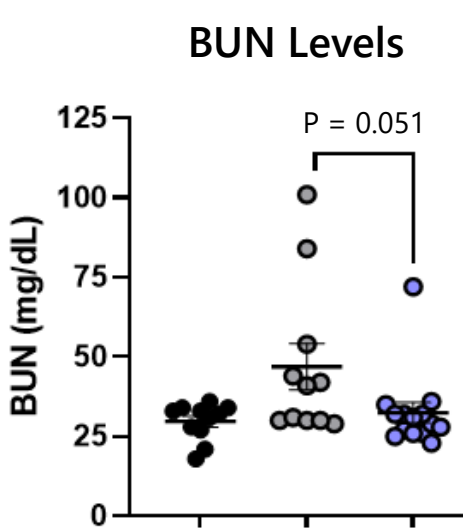
● No Disease Control

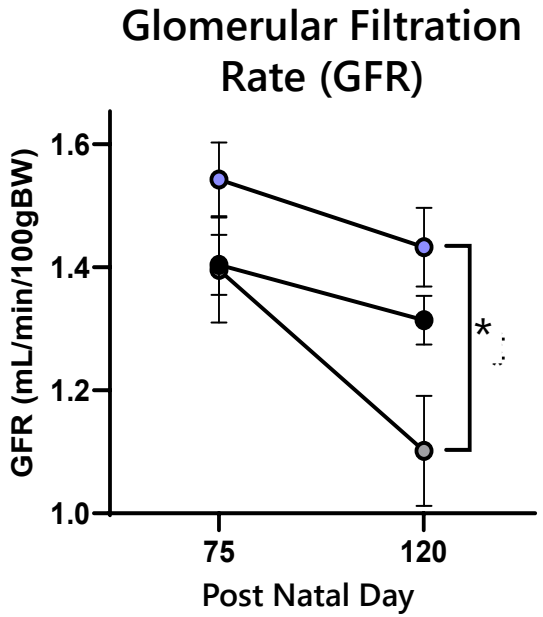
● ADPKD2 Cystic Disease Control

● TQB-001 Treated Animal



Kidney Function Assays





● No Disease Control

● ADPKD2 Cystic Disease Control

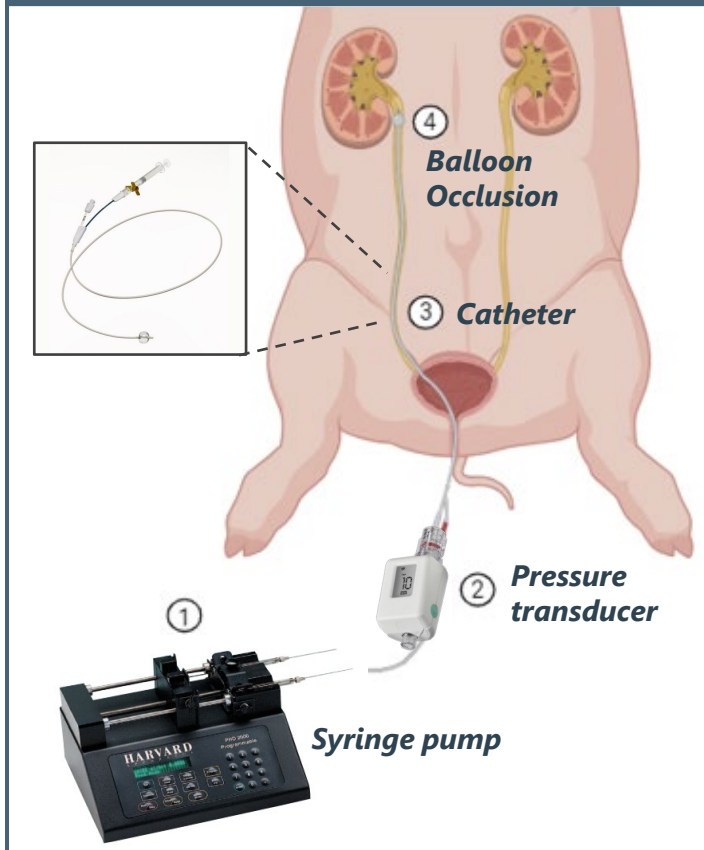
● TQB-001 Treated Animals

TQB-001 prevents kidney function loss

$Pkd2^{fl/fl}$, $Pax8\text{-}rtTA^{+/}$, $TetO\text{-}Cre^{+/}$ mouse model, where doxycycline treatment knocks out PC2 expression specifically in kidney tubules by excising exons 11-13 in Pkd2 gene.
Representative H&E kidney images from each group, 1x magnification.
Treatment was performed with an HA-tagged version of TQB-001

Direct Kidney Delivery via Retrograde Ureteral Administration (RUA)

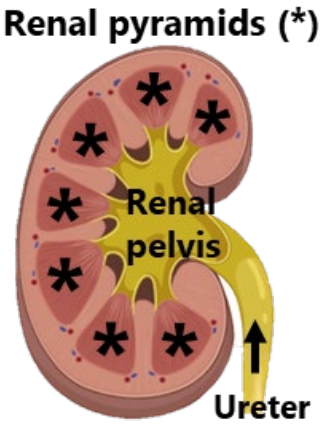
RUA Delivery in Pigs



Defined RUA Delivery Parameters

Defined Parameters:

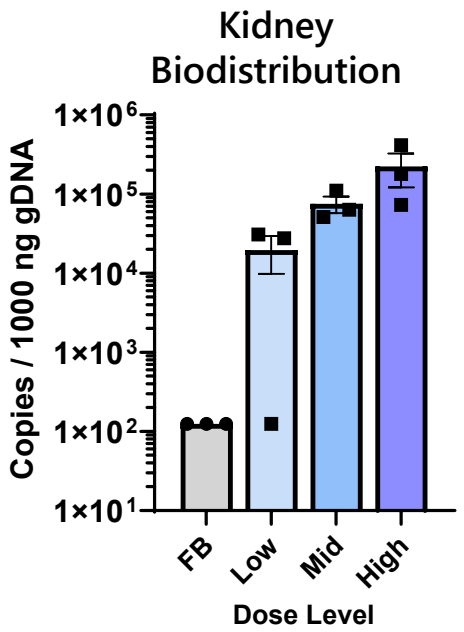
- Volume
- Injection Rate
- Dwell Time

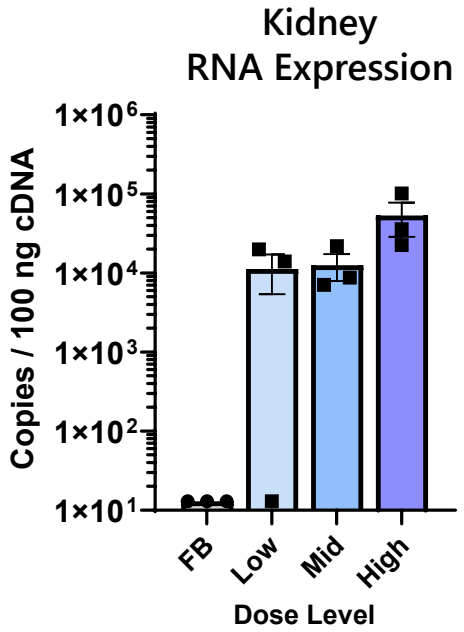


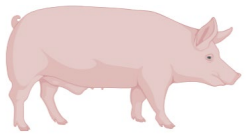
RUA enables direct AAV delivery to kidney nephrons — leveraging an established clinical procedure enhanced by Torque's proprietary delivery protocol

TQB-001 Robustly and Safely Transduces Kidney following RUA Delivery

Pig Dose Range Finding (DRF) Study Design
Naïve Female Farm Pigs



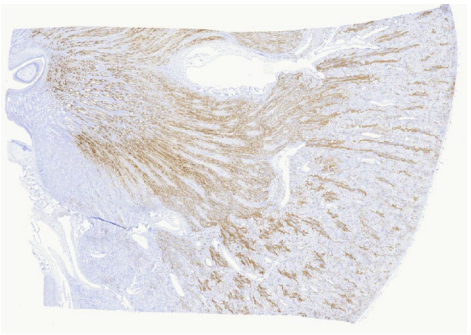


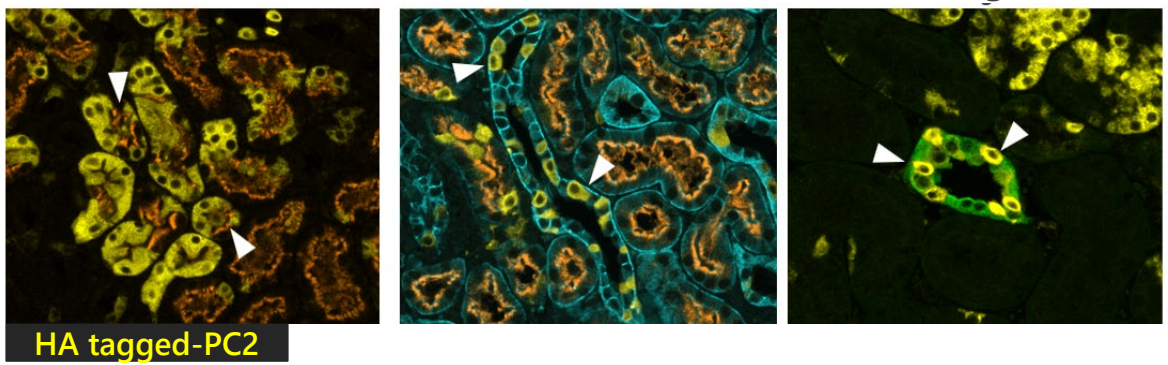


- All animals dosed **bilaterally** via RUA
- All dose levels were **well-tolerated**
- **Limited systemic exposure**: 50-fold less RNA expression in liver vs kidney at mid-dose

TQB-001 Kidney Protein Expression

IHC for HA-tagged PC2 in kidney (mid dose)





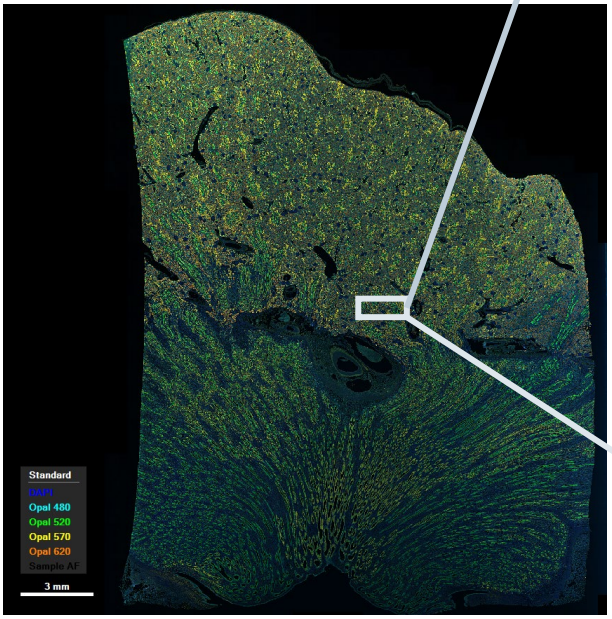
TQB-001 is expressed in key cell types throughout the kidney

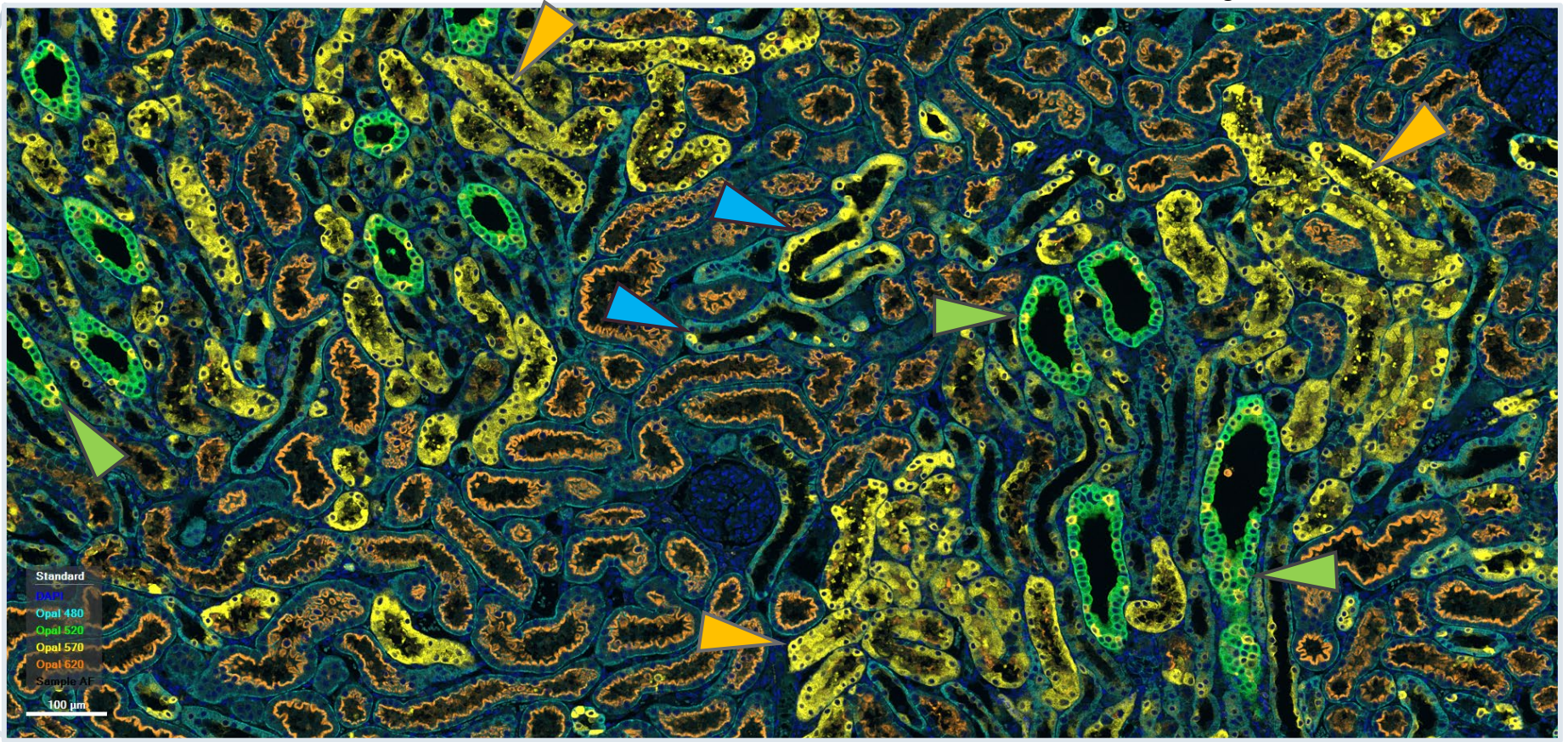
HA-tagged version of TQB-001 used in these studies. Pigs were immunosuppressed (prednisone) before and during study and necropsied 28 days post-AAV treatment.
Lower limit of quantitation (LLOQ): 5000 copies / 1000 ng gDNA and 600 copies / 100 ng cDNA for biodistribution and RNA expression, respectively.
Immunohistochemistry performed using an HA-antibody for PC2-HA; exemplar image from mid-dose group
Immunofluorescence images from pigs dosed unilaterally with HA-tagged TQB-001; Tag+: HA-positive; LRP2: Proximal Tubules; ECAD+/LRP2-: Distal Tubules; AQP2: Collecting Ducts

TQB-001 Expression Consistently Observed in All 3 Key Kidney Cell Types

Immunofluorescence (IF) of PC2-HA Co-Stained with Kidney Cell Markers

High Dose (Left Caudal Pole)





PC2-HA Expression
Collecting Duct
Proximal Tubule
Distal Tubule

Immunofluorescence images from pigs dosed bilaterally with HA-tagged TQB-001; Tag+: HA-positive
Proximal Tubule: LRP2+, ECAD+, AQP2-; Distal Tubule: LRP2-, ECAD+, AQP2-; Collecting Duct: LRP2-, ECAD+, AQP2+

ADPKD1 Program Leverages Torque's AAV-Encoded Circular RNA Technology

RATIONALE

- Loss of PC1 expression drives cystic phenotype in kidney tubule cells.
- *Pkd1* mRNA is a miR-17 target.
- Inhibiting miR-17 increases PC1 expression and alleviates cystogenesis.

STRATEGY

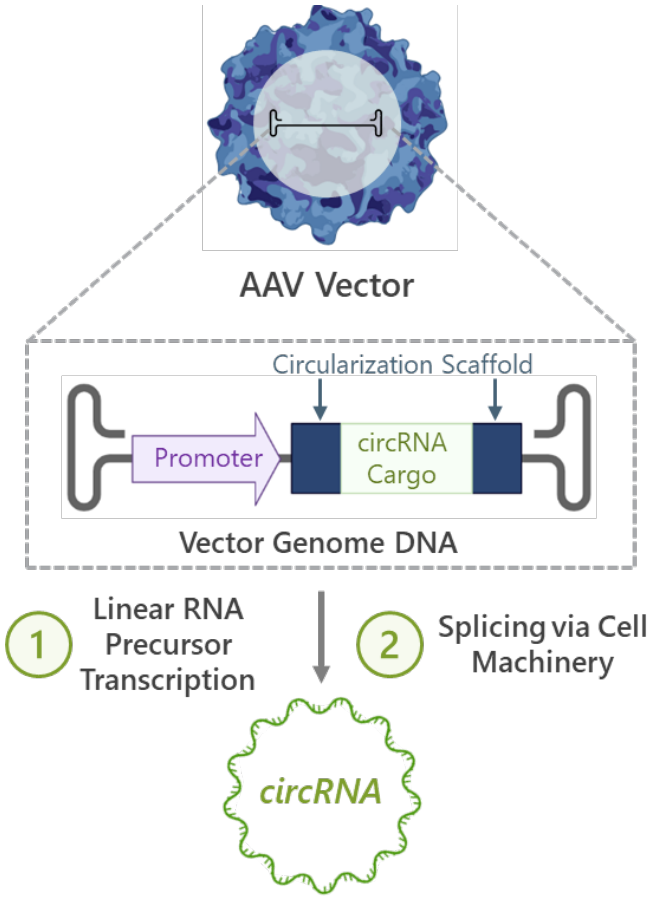
- Expression of a circRNA miR-17 inhibitor from an AAV vector delivered directly to the kidney to increase PC1 expression.

Program Development

Discovery → *In vivo* PoC → DRF Studies → IND Enabling Activities → IND Submission and FIH Trial

Current Stage

AAV:circRNA

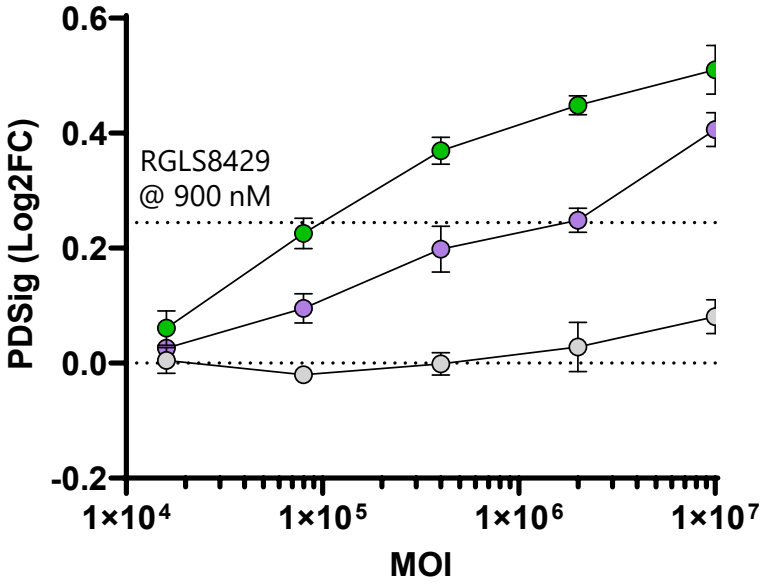


PC1; polycystin-1 protein

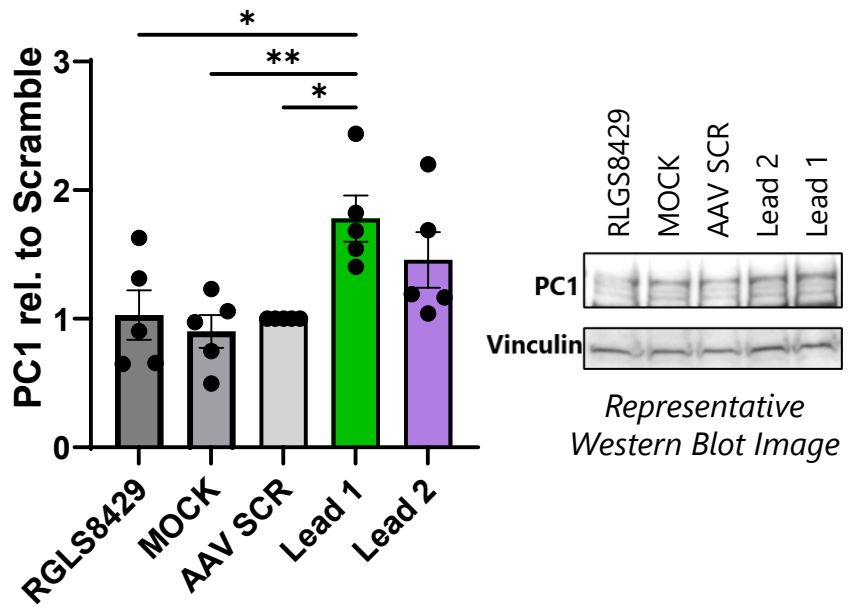
ADPKD1 Lead Vectors are Biologically Active in Patient Cells

In Vitro miR-17 Inhibition

miR-17 Target Panel RNA Expression



PC1 Protein Expression



Representative Western Blot Image

Scramble Control Lead 1 Lead 2

Lead vectors increase miR-17 target gene and PC1 expression, ***demonstrating miR-17 inhibition***

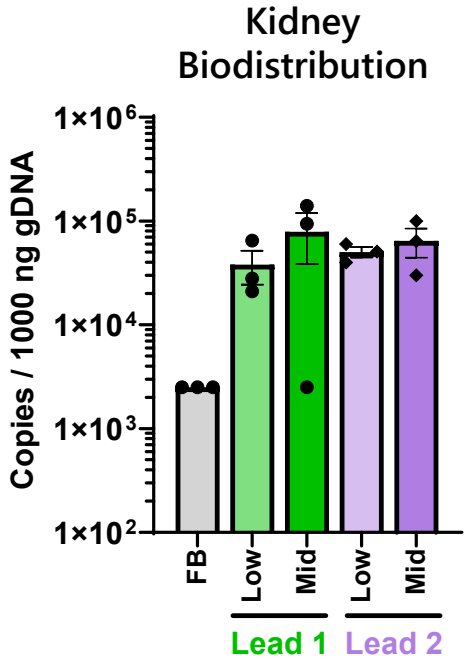
Activity at high MOIs is similar or exceeds that observed from positive control oligo (RGLS8429)

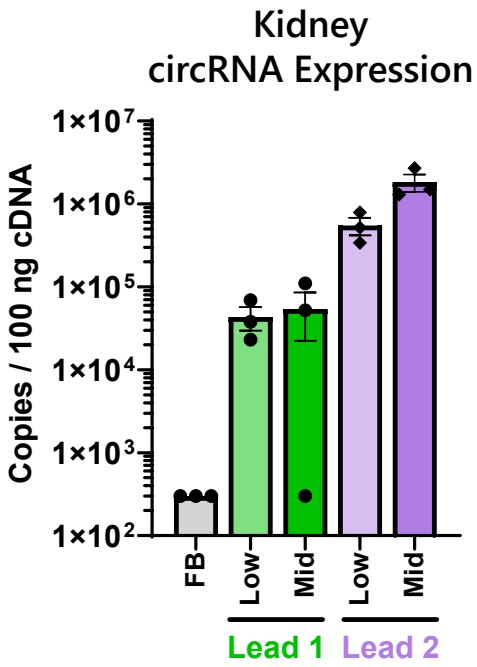
In vivo studies in ADPKD1 mouse models are ongoing

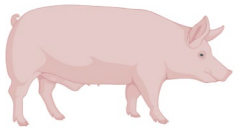
WT 9-7 patient-derived cells (PKD1 +/-; truncating Q2665X mutation)
PDSig measures the expression of seven miR-17-responsive genes
** p < 0.05, ** p < 0.01*

AAV:circRNAs are Robustly and Safely Expressed in the Pig Kidney via RUA

Pig Dose Range Finding (DRF) Study Design
Naïve Female Farm Pigs

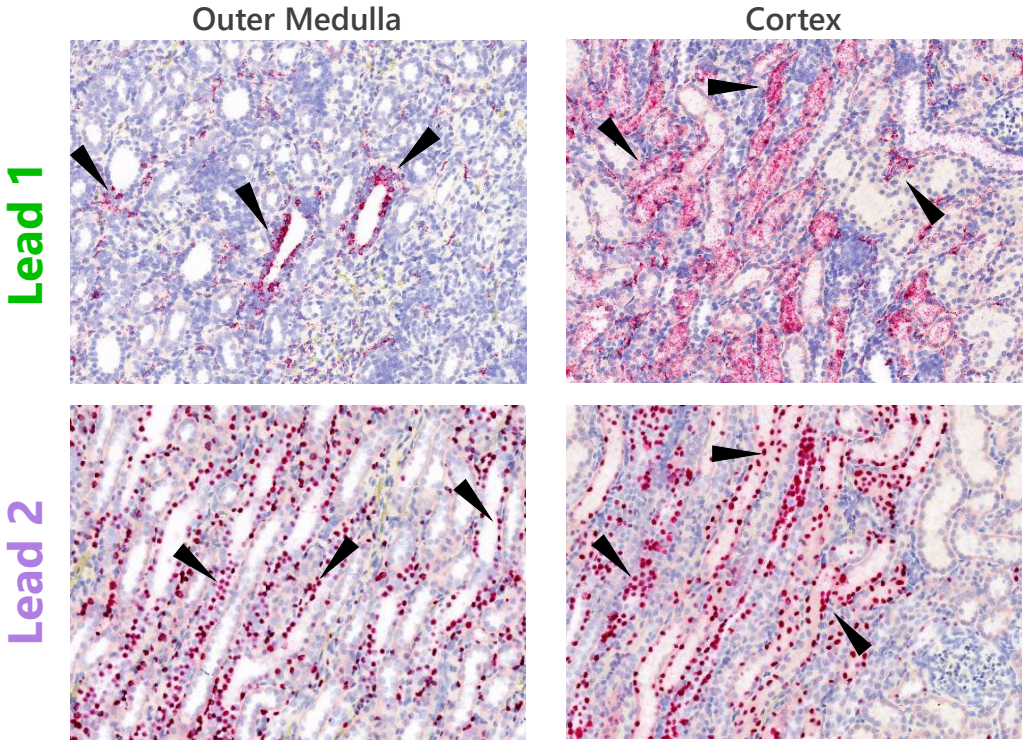






- All animals dosed **bilaterally** via RUA
- All dose levels were **well-tolerated**
- **≥90%** of transcripts converted to circRNA

Kidney circRNA Expression (*In situ* hybridization)

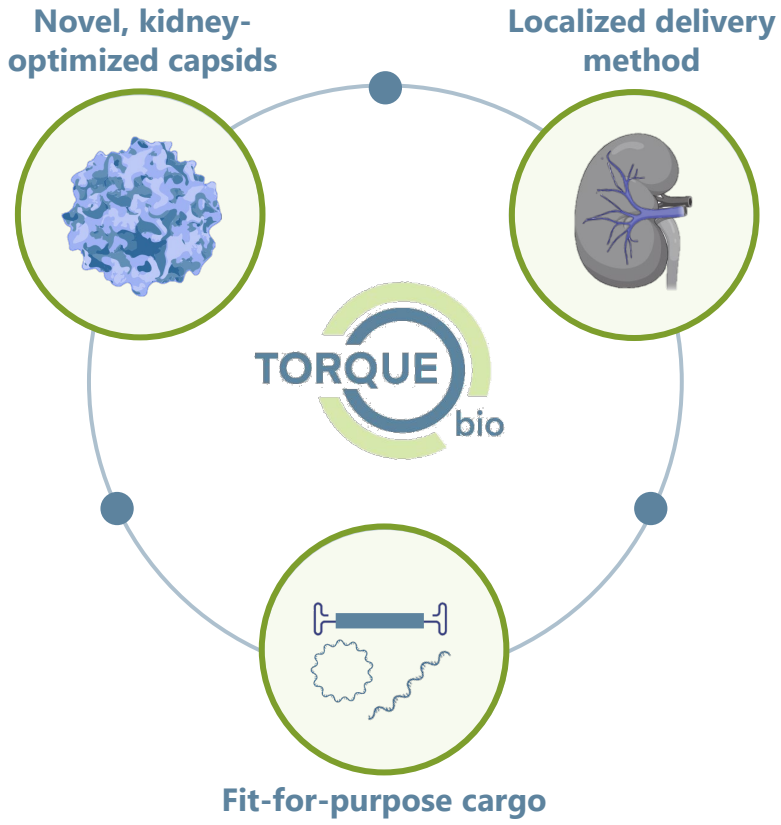


AAV:circRNAs are expressed in key cell types throughout the kidney

Pigs were immunosuppressed (prednisone) before and during study and necropsied 28 days post-AAV treatment.
Lower limit of quantitation (LLOQ): 5000 copies / 1000 ng gDNA and 600 copies / 100 ng cDNA for biodistribution and RNA expression, respectively.
Representative images from pigs dosed at mid dose. ISH = in situ hybridization

Pioneering New Kidney-Targeted AAV Gene Therapies for ADPKD Patients

Approach uniquely designed to overcome the historical barriers in renal gene therapy



Novel Kidney-Targeted AAV Platform

- Engineered AAVk.20 capsid achieves enhanced kidney transduction across species
- AAV-encoded circular RNA modality enables durable, programmable renal gene expression

Preclinical Efficacy Across Two ADPKD Programs

- TQB-001 (PKD2 gene replacement): >35% cyst burden reduction with preservation of kidney function in ADPKD2 mice
- AAV:circRNA (miR-17 inhibition): inhibits miR-17 activity and restores PC1 expression in ADPKD1 patient-derived cells

Clear Translational Path to the Clinic

- Localized kidney delivery (RUA) achieves high renal transduction with limited systemic exposure
- IND-enabling studies underway, supporting advancement toward clinical evaluation

Acknowledgments

Torque Bio

Travis Gulledge
Trevor Gonzalez
Colin O'Banion
Erin Borchardt
Shataakshi O'Neil
Georgios Vasilakos
Abra Chaney
Della Vanko
Tacia Small
Isaac Mick
Andrew Hale
Jonas Onuoha
Jeffery Greenland
Aaron Hall
Roxanne Armstrong
Brian Bettencourt
Natalia Reim Rodriguez
Heather Vincent
Michael Mercaldi

University of Maryland School of Medicine

Patricia Outeda Garcia

Contact: amy@torquebio.com