tengion®

Regenerative medicine brought to life.

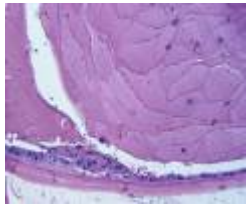
Discovery and development of regenerative medicine products comprised of autologous cells and biomaterials

ISCT
September 28, 2010
San Francisco, CA

Tengion's products catalyze regeneration

INPUTS

Biomaterials



Cells

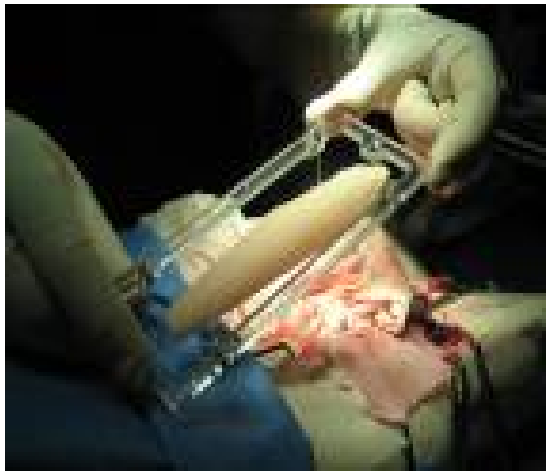
Bioprocess

Delivery Systems

INTEGRATED PLATFORM

OUTPUTS

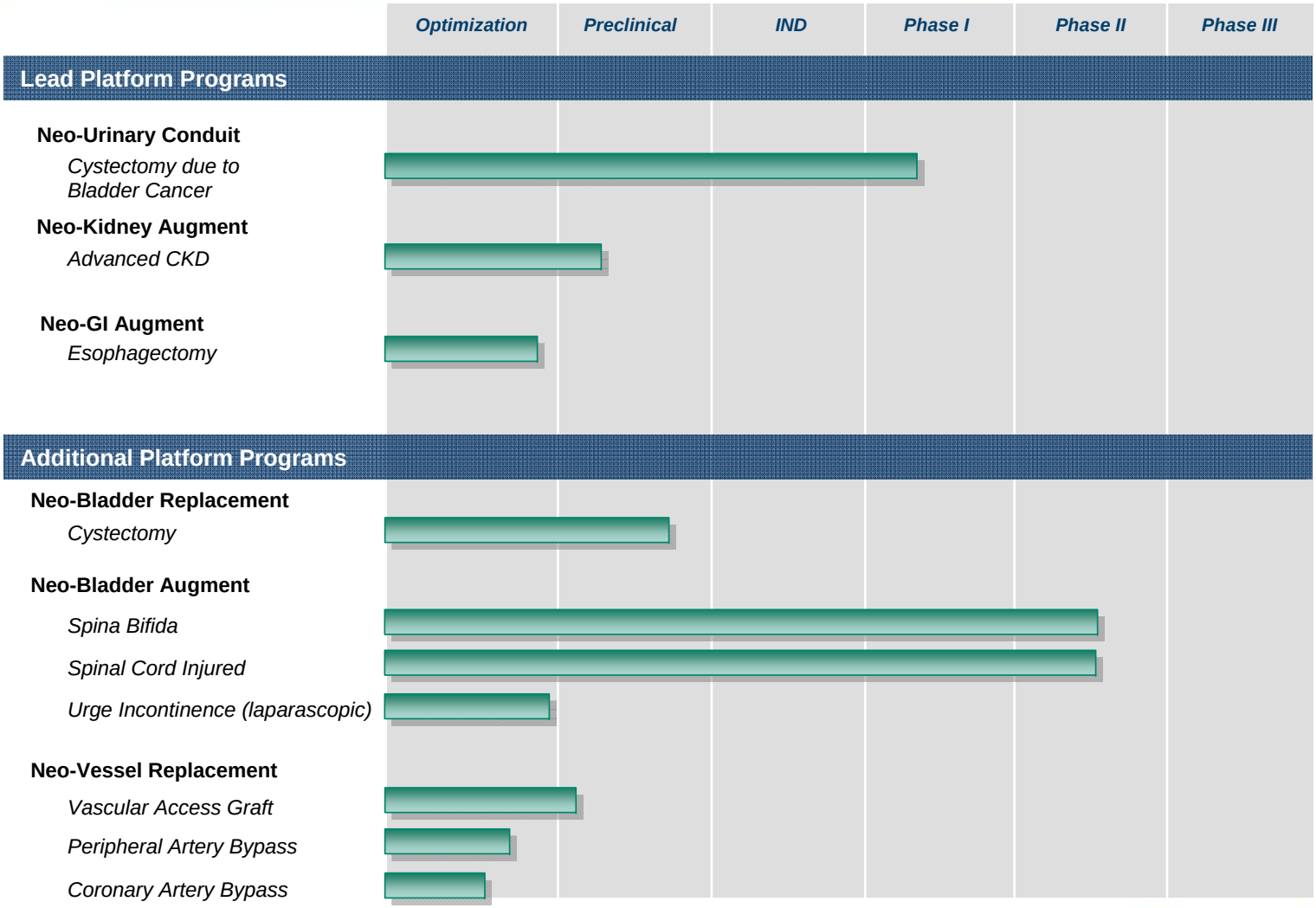
Regenerative Templates



- ***Combination products***
- ***Stimulate regeneration***
- ***Integrate into host***

tengion®

Tengion Product Pipeline



Accelerating development timelines
for Clinical Translation of regenerative medicine products

Iterative *in vitro & in vivo* testing of early-stage prototypes

- ***Rapid identification of bioactive components and candidate product prototypes***

Strategic optimization of bioprocess

- ***Continuous improvement of lead product candidates through development***

Preclinical development in clinical context

- ***GMP-compliant bioprocess, composition, and clinically-supported delivery system***

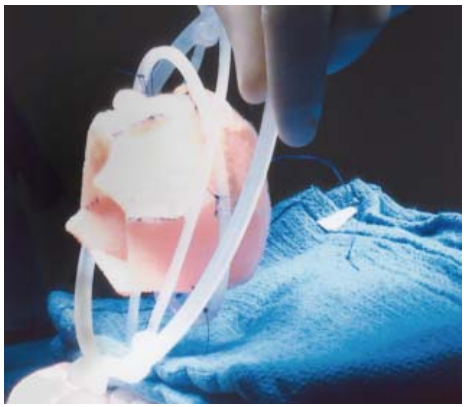
Bringing forward the simplest solution to address unmet medical needs safely and efficaciously

tengion®

Regenerating urinary tissue for unmet needs
From bladder augmentation to urinary conduit

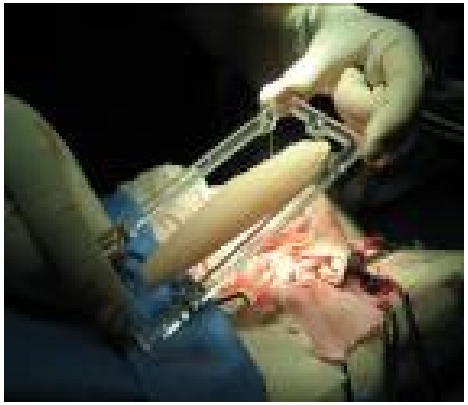
Neo-Bladder Augment

- *Augments function of neurogenic bladder*
- *PLGA scaffold + bladder-derived urothelial cells & smooth muscle cells*
- *Regenerates bladder tissue*



Neo-Urinary Conduit

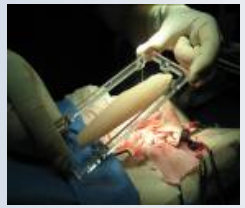
- *Provides exit for urine after bladder removal due to cancer*
- *PLGA scaffold + adipose-derived smooth muscle cells*
- *Regenerates urinary tissue*



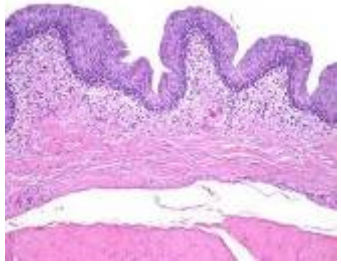
tengion®

Neo-Urinary Conduit – Preclinical Data (GLP n=66)

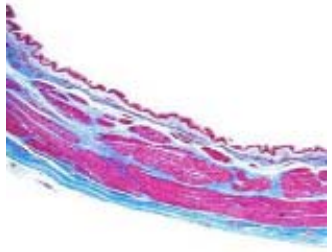
Regeneration with urine flow in a swine model



Native-like regeneration at three months

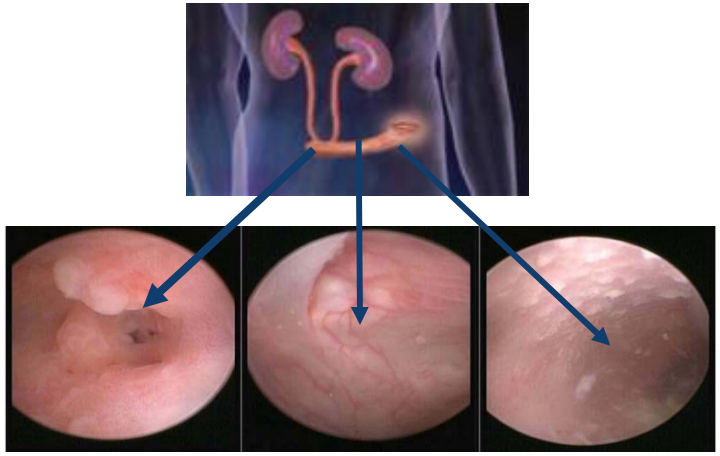


Normal lining



Normal thickness and muscle structure

Regeneration of normal lining from ureters to skin with no urine absorption and no mucus secretion



Junction with ureter

Conduit

Junction with skin

The product catalyzed regeneration of a conduit made of bladder tissue, allowing for unobstructed urine flow

tengion®

Source: Tengion IND #14218; Presented at International Society for Stem Cell Research, 2009

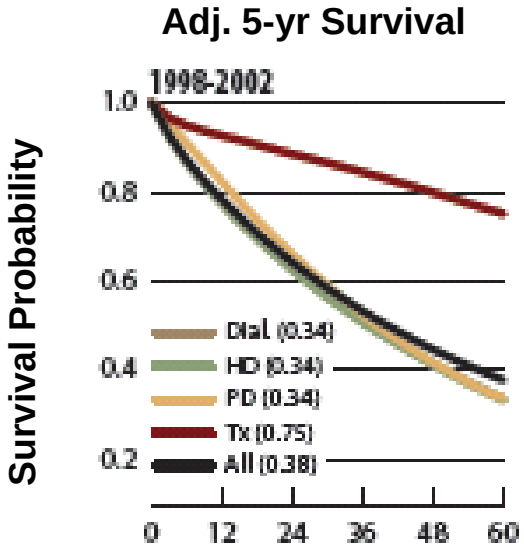
Neo-Urinary Conduit
Regulatory pathway to approval

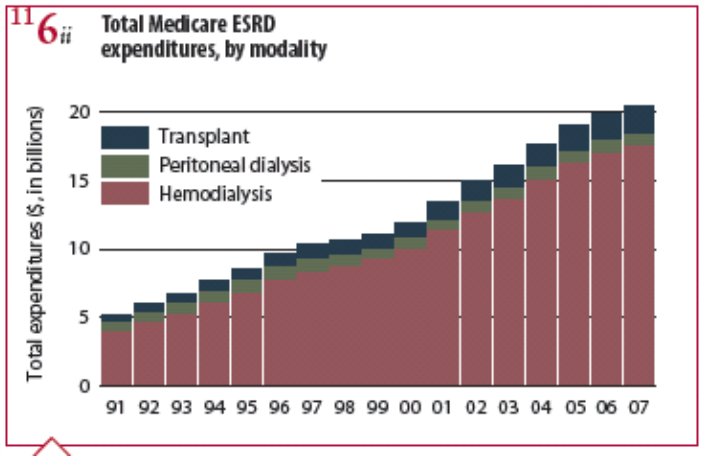
FDA

- *BLA pathway, CBER leads and CDRH collaborates*
- *IND approved within 30 days*
- *Frequent interactions with FDA since discovery*
- *Orphan designation may be applicable in the future*
- *US manufacturing facilities may be suitable through commercialization*

Neo-Kidney Augment™ (NKA)

Chronic Renal Failure is a leading cause of death worldwide





- ***>350,000 people with end-stage renal disease (ESRD)***
- ***>50,000 people with ESRD are waiting for kidney transplants in the US***
- ***>100,000 people start dialysis annually in the US***
  - *$60,000 1st year cost*
  - *$22 billion in Medicare direct costs annually*
- ***New treatment modalities are needed***

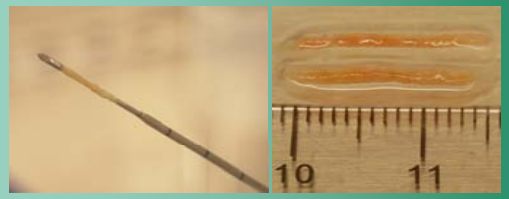
tengion®

2009 US Renal Data System, Annual Data Report Vol 2
"Atlas of ESRD"

Neo-Kidney Augment™ (NKA)

Applying Tengion's regenerative platform to a solid organ

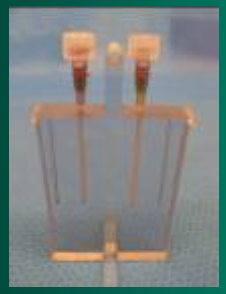
Bioactive Renal Cells from Kidney Biopsy



Isolation / Expansion of ABI

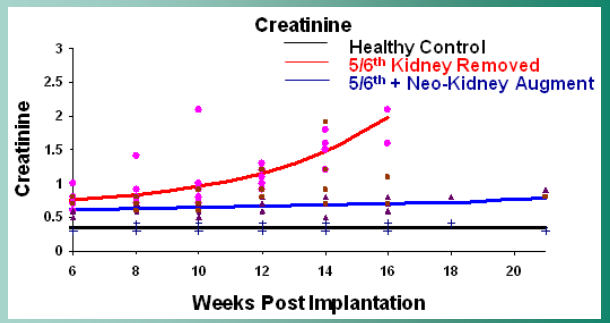
Bioreactor System for NKA Production*

Injectable Delivery System*



***In vivo* Delivery**

Functional Regeneration**



tengion®

**Kelley et al, Am J Physiol Renal Physiol 2010 (Published online 9/6/2010)

*In development

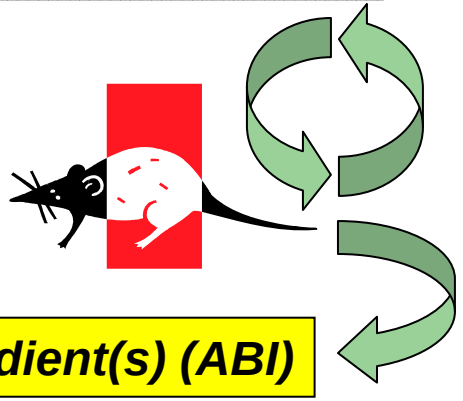
Strategic approach to identify essential components *of Neo-Kidney Augment™ (NKA) prototypes*

Generate testable array of 'kidney components' based on native tissue composition

Design combinatorial experiments based on functional component characteristics

Prototypes Tested	B1	B2	B3	B4	B5	BM1	BM2	BM3	BM4
1	■				■				
2		■							
3			■						
4				■					
5		■	■						
6		■		■					
7			■	■					
8	■	■	■	■	■				
9	■	■	■	■	■	■			
10		■				■			
11		■					■		
12		■						■	
13		■							■
14				■		■			
15				■			■		
16				■				■	
17						■			
18									■
NO TREATMENT									
NO DISEASE									

Iterative in vitro and in vivo testing in models of CKD



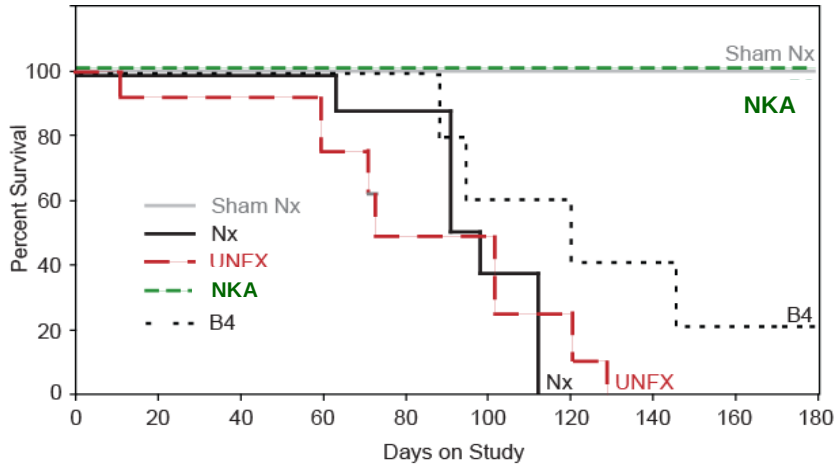
Identification of Active Biologic Ingredient(s) (ABI)

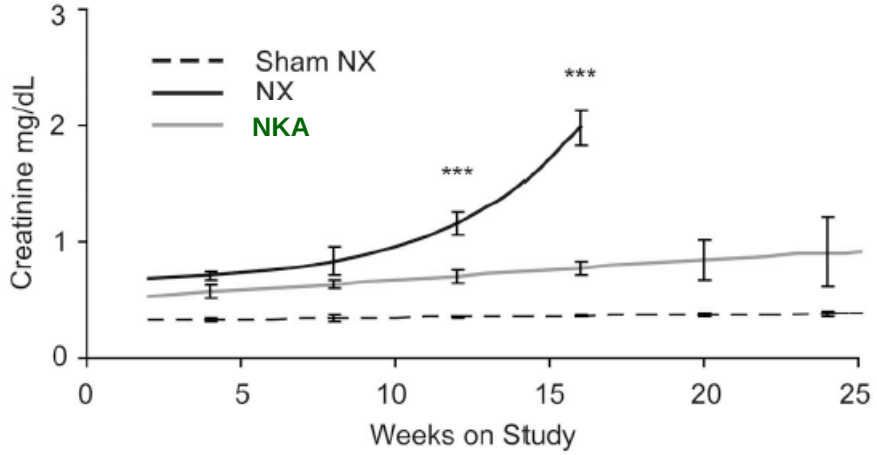
tengion®

Cellular ABI for NKA validated in vivo
In rodent 5/6 nephrectomy model of chronic renal failure

- ***NKA ABI delivered after chronic disease state established***
  - *sCREAT sustained at >200%*
  - *BUN sustained at >150%*

- ***Selected ABI (NKA) outperforms unfractionated mixture (UNFX) and improves multiple physiologic parameters***
  - *Enhanced Survival*
    - *(100% (NKA) vs. 0% (Nx and UNFX)*
  - *Stabilized filtration (sCreatinine)*
  - *Improved protein retention*
  - *Reduced phosphatemia*





tengion®

NKA provides structural and functional regeneration

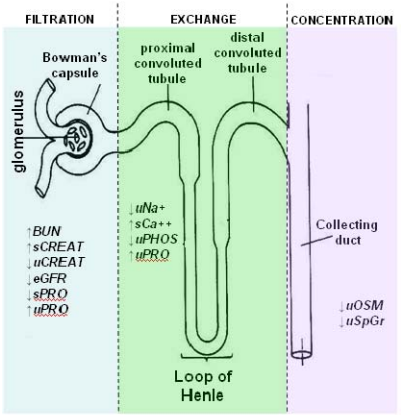
Systemic endpoints correlate with durable tissue-level improvements

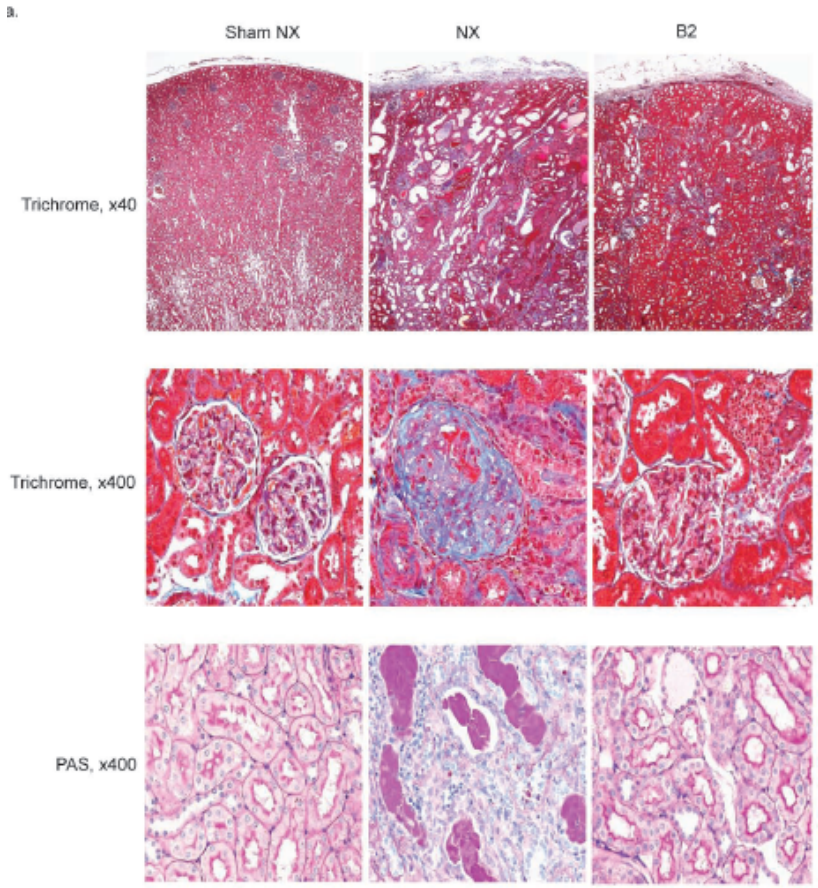
Functional regeneration

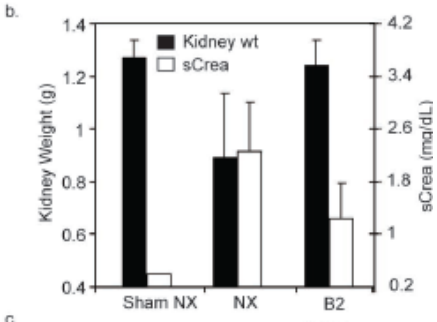
- ***Glomeruli***
- ***Tubules***

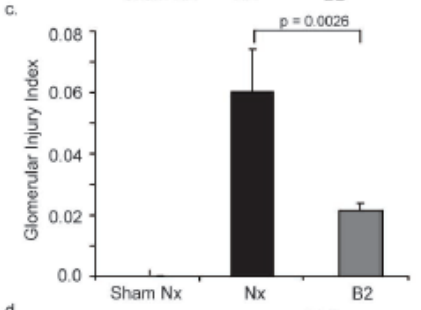
Reduced fibrosis

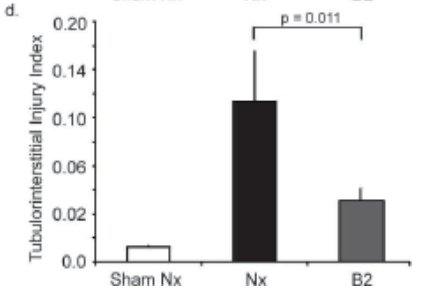
- ***Glomerular***
- ***Tubulointerstitial***











tengion®

Validation of NKA ABI function in additional models
Increases probability of success through development

- ***NKA ABI validated in 5/6 Nx rodent model of CKD due to renal mass insufficiency****
  - *Robust therapeutic effect*
  - *Reproducible across independent studies*

- ***Will the NKA ABI function in a model of CKD secondary to obesity and Type 2 Diabetes?***
  - *Active investigation of NKA ABI in rodent ZSF1 model of obesity, Type 2 Diabetes, and hypertension*
    - *Evaluation of intervention at CKD Stages 3-4*
    - *NKA ABI derived from diseased donors*

- ***Will the NKA ABI function in a large animal model of CKD?***
  - *Active investigation of NKA ABI in canine model of CKD*
    - *Surgically-induced remnant kidney model of renal insufficiency*
    - *Autologous cells delivered via minimally-invasive means*

tengion®

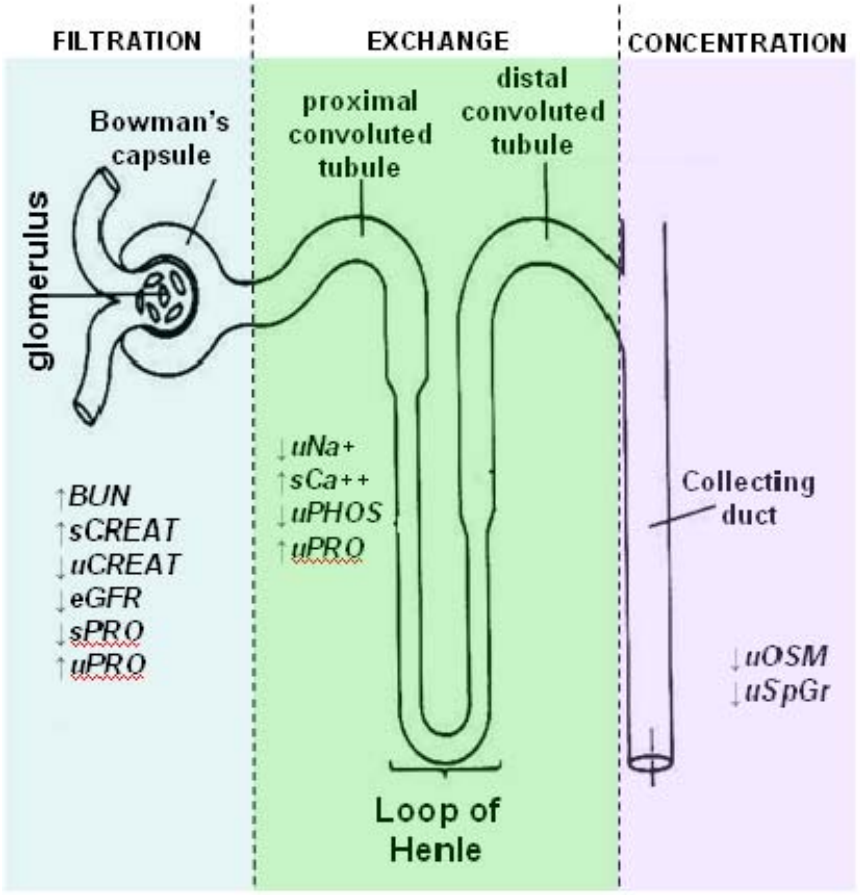
*Kelley et al, Am J Physiol Renal Physiol 2010 (Published online 9/6/2010)

Obese ZSF1 rats model progressive nephropathy

Renal disease secondary to diabetes mellitus and hypertension

Aggressive Metabolic Disease

- *~50% mortality at ~1yr*
- *Multiple co-morbid conditions*
  - *Hyperglycemia*
  - *Vasculopathy*
  - *Hypertension*
- *Progressive disease occurs throughout the nephron*
  - *Renal hypertrophy*
  - *Progressive glomerular sclerosis*
  - *Progressive decline in GFR*
  - *Tubular / interstitial fibrosis*
  - *Severe proteinuria*

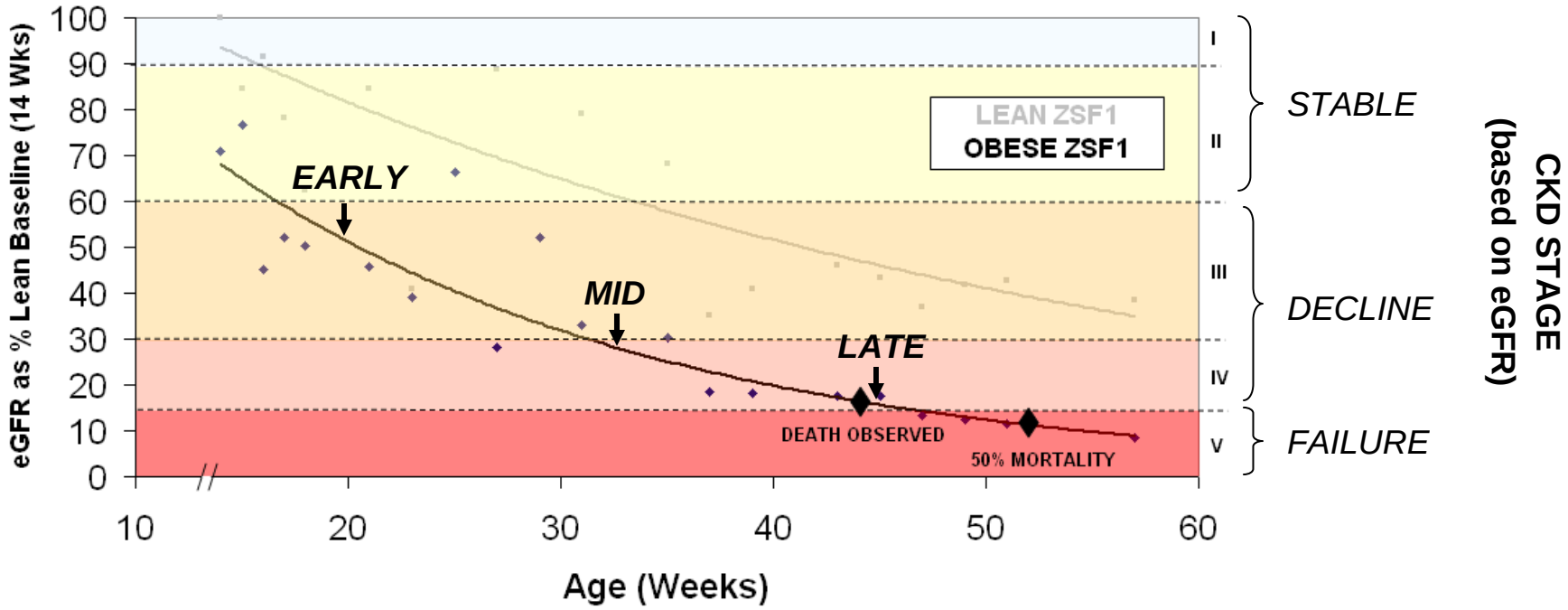


tengion®

Tofovic et al., Ren. Fail. 22:387 (2000)

Validating NKA ABI in chronic disease

Renal failure secondary to obesity and Type 2 diabetes (ZSF-1)



Intervention windows:

- ***EARLY (Early Stage 3 CKD)***
- ***MID (Late Stage 3 CKD) w/ moderate control of hyperglycemia***
- ***LATE (Late Stage 4 CKD) w/ moderate control of hyperglycemia***
- ***Lean ZSF1 = positive control***

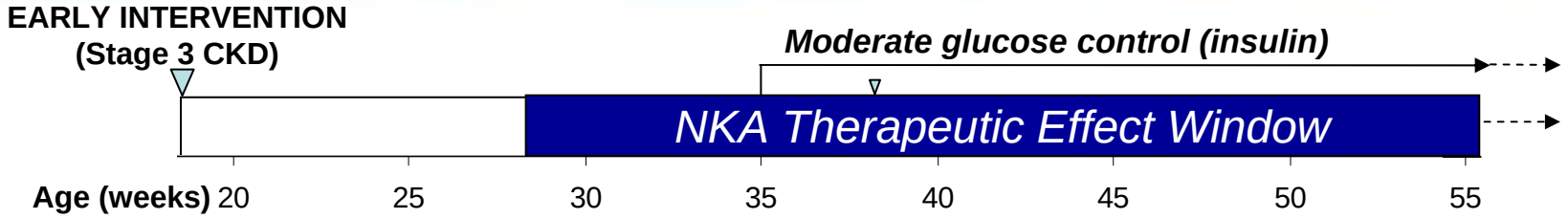
Intervention strategies:

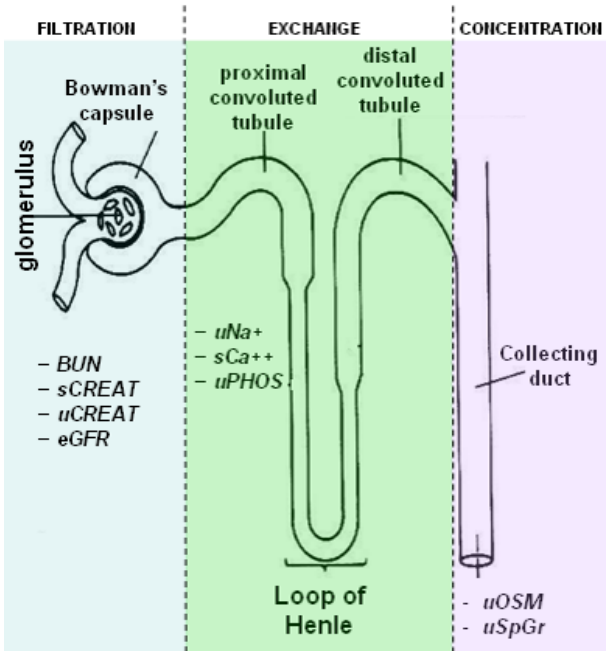
- ***Syngeneic diseased donors***
- ***Treated (1) or both kidney(s)***

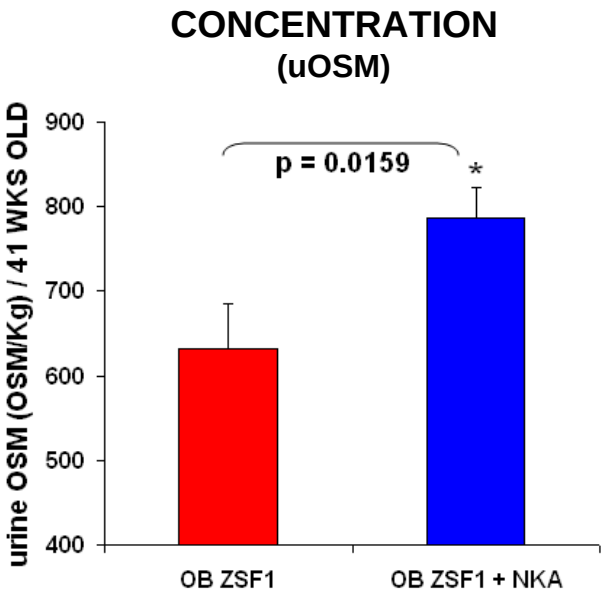
tengion®

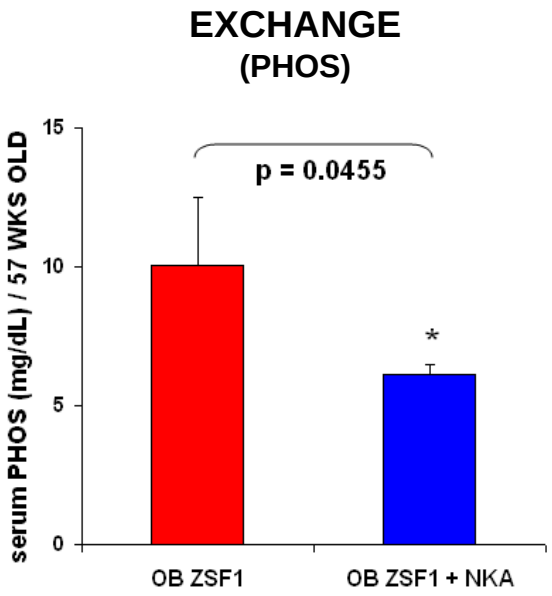
NKA ABI improved function throughout the nephron

Collecting ducts, tubules, and glomeruli



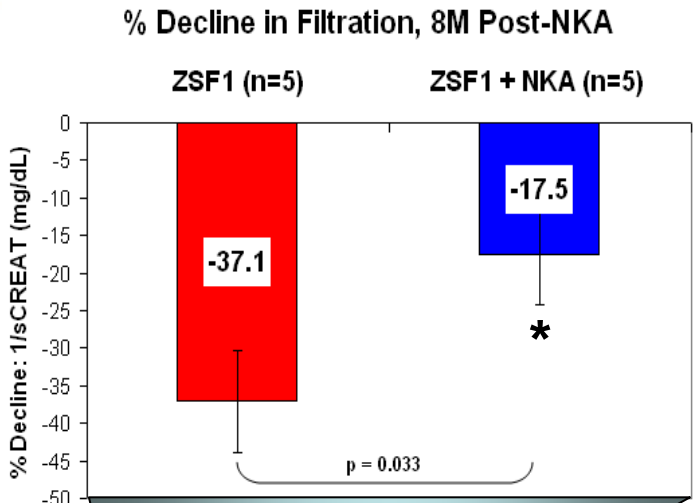


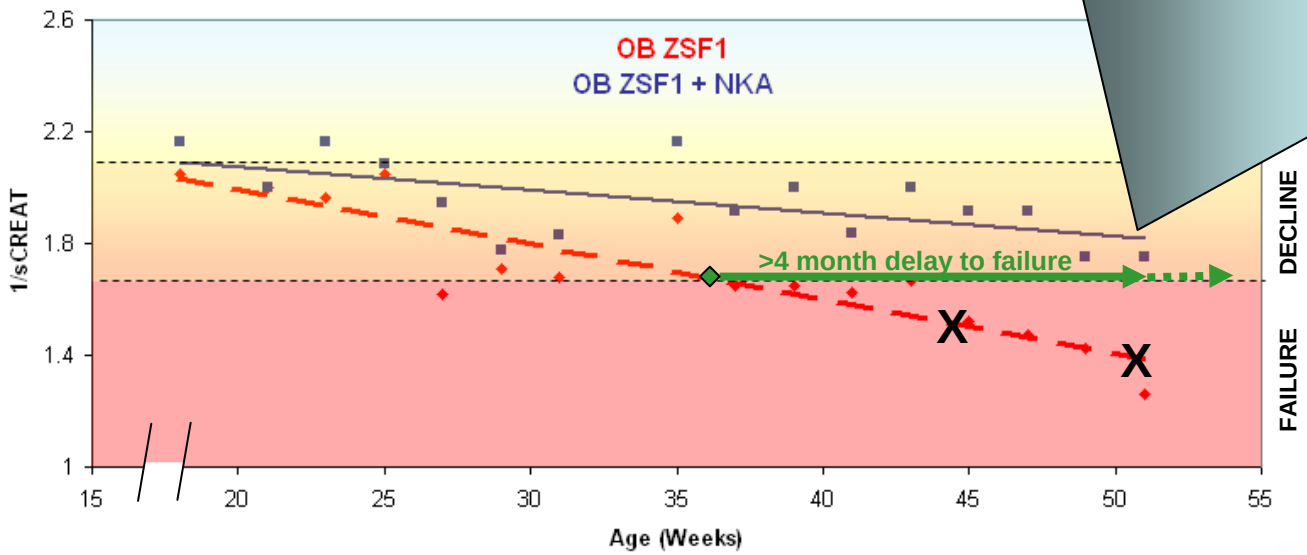




NKA ABI preserved renal filtration function
For up to 8 mo post-treatment (ZSF-1)

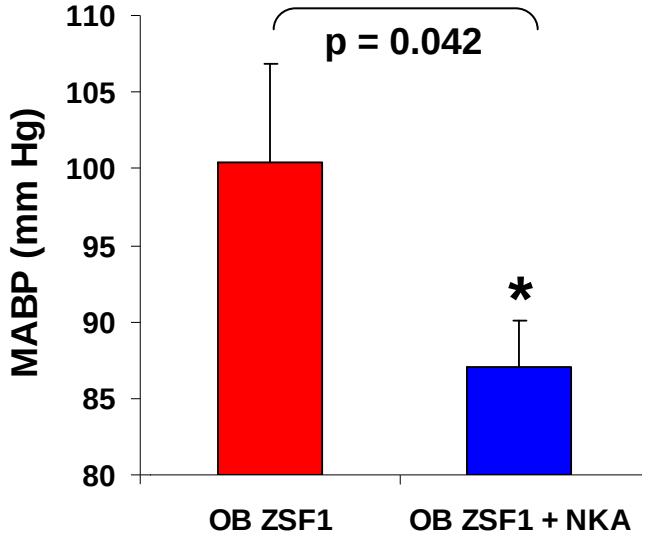
- ***NKA provided >50% reduction in filtration loss over 8 months duration***
- ***Delayed progression to 'Failure' (CKD 5) by at least 4 months***
  - *OB ZSF1 progressed to CKD 5 at 36 wks*
  - *OB ZSF1 + NKA delayed progression to at least 52 wks*
    - *16 wks = ~30% of OB ZSF1 lifespan*





NKA ABI reduced hypertension and improved survival
ZSF1 rats at >1 year of age

- ***NKA reduced mean arterial blood pressure (MABP) significantly at 57 weeks of age***



- ***NKA supports survival beyond 50% mortality time point for OB ZSF1***

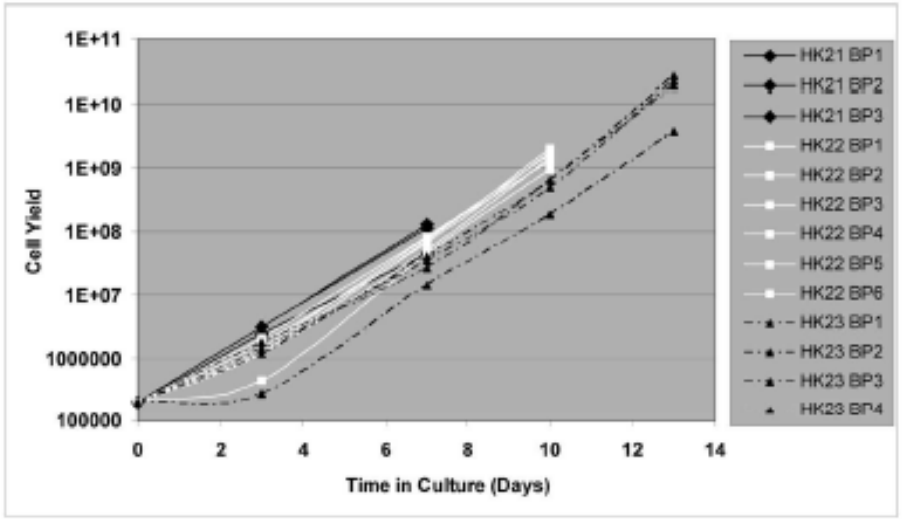
Treatment Group	*57-week Survival*
OB ZSF1	40% (2/5)
OB ZSF1 + NKA ABI	100% (5/5)

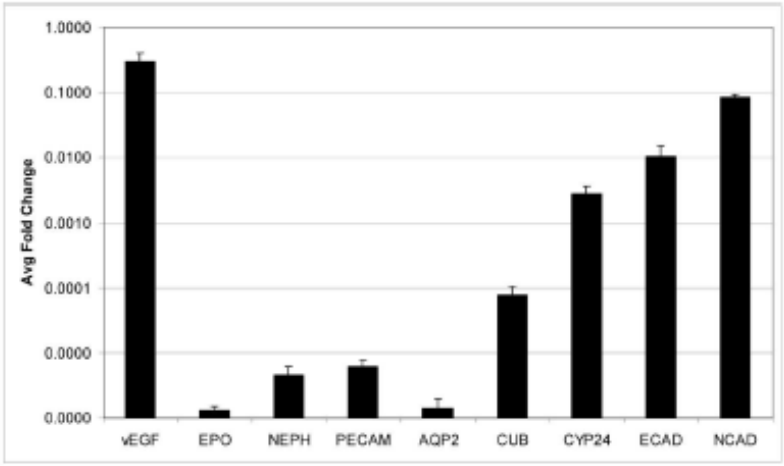
tengion®

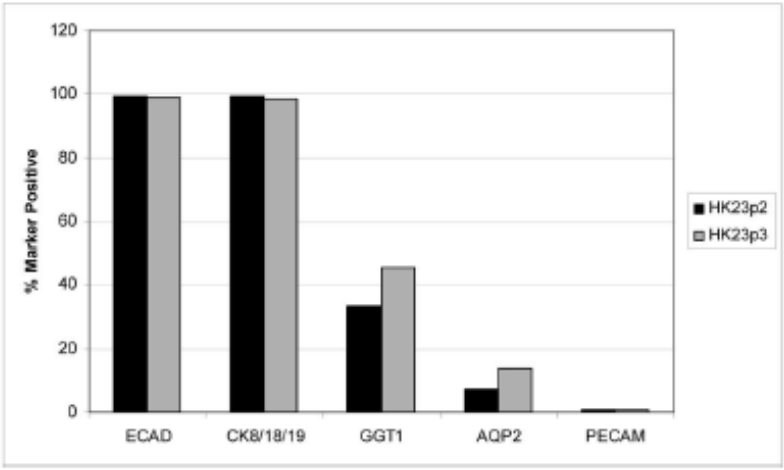
Translation of NKA ABI

Isolation, characterization, & expansion from human CKD-derived kidney tissue

- ***Standard core needle biopsy procedure (0.02g tissue)***
- ***Cells can be expanded and cryopreserved***
- ***Salient phenotypic attributes are preserved***
- ***Supports autologous sourcing strategy***







tengion®

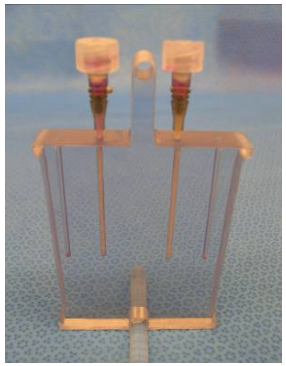
Development of NKA product candidate
To target delivery, increase stability, and expand use

Product Candidate

- Formulated for targeted delivery, stability, durability and function of the ABI

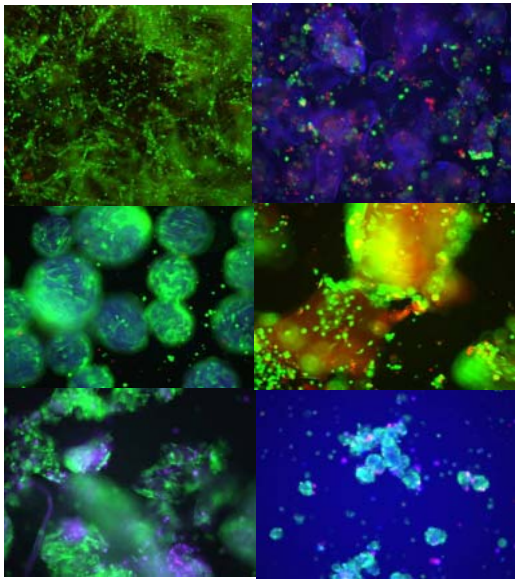
Delivery System

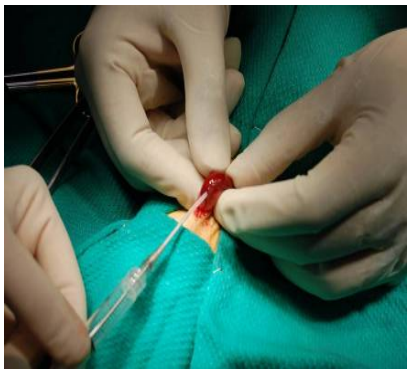
- Bioreactor system for stable transport and delivery of product



Clinical Testing – Surgical Options

- Laparotomy (open procedure)
- Laparoscopic (ultrasound guided)





tengion®

Summary

- *NKA ABI function verified* in vivo *in two rodent models of CKD*
  - *5/6 Nx-induced renal failure*
  - *Severe diabetic nephropathy*

- *Successful translation of NKA ABI isolation, characterization, & expansion processes*
  - *Diseased rodent donors*
  - *Large animal (swine and canine)*
  - *Human (non-CKD and CKD-derived)*

- *Ongoing development of NKA product candidates drives*
  - *Optimal product formulation (e.g., shelf life)*
  - *Safe and targeted* in vivo *delivery*
  - *Maximize regenerative response to delay CKD progression*

tengion®


tengion®
Regenerative medicine
brought to life.