

tengion<sup>®</sup>

Regenerative medicine  
brought to life.

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

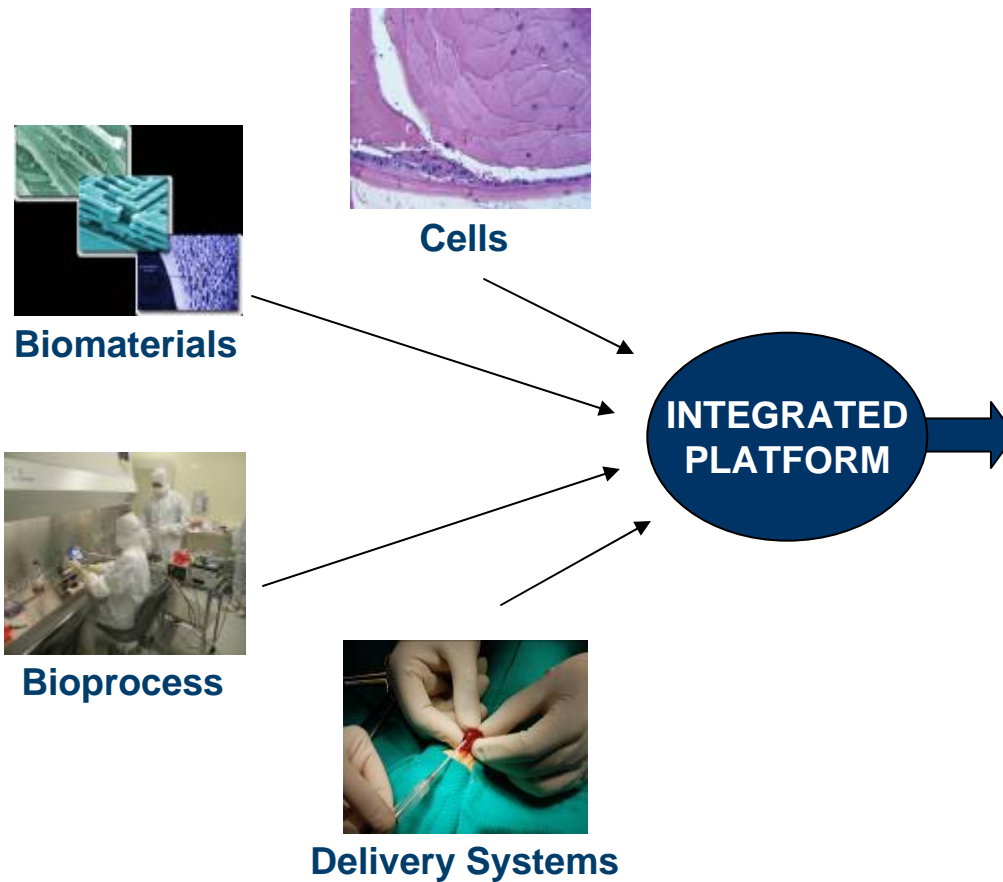
***ISCT***

***September 28, 2010***

***San Francisco, CA***

# Tengion's products catalyze regeneration

## INPUTS



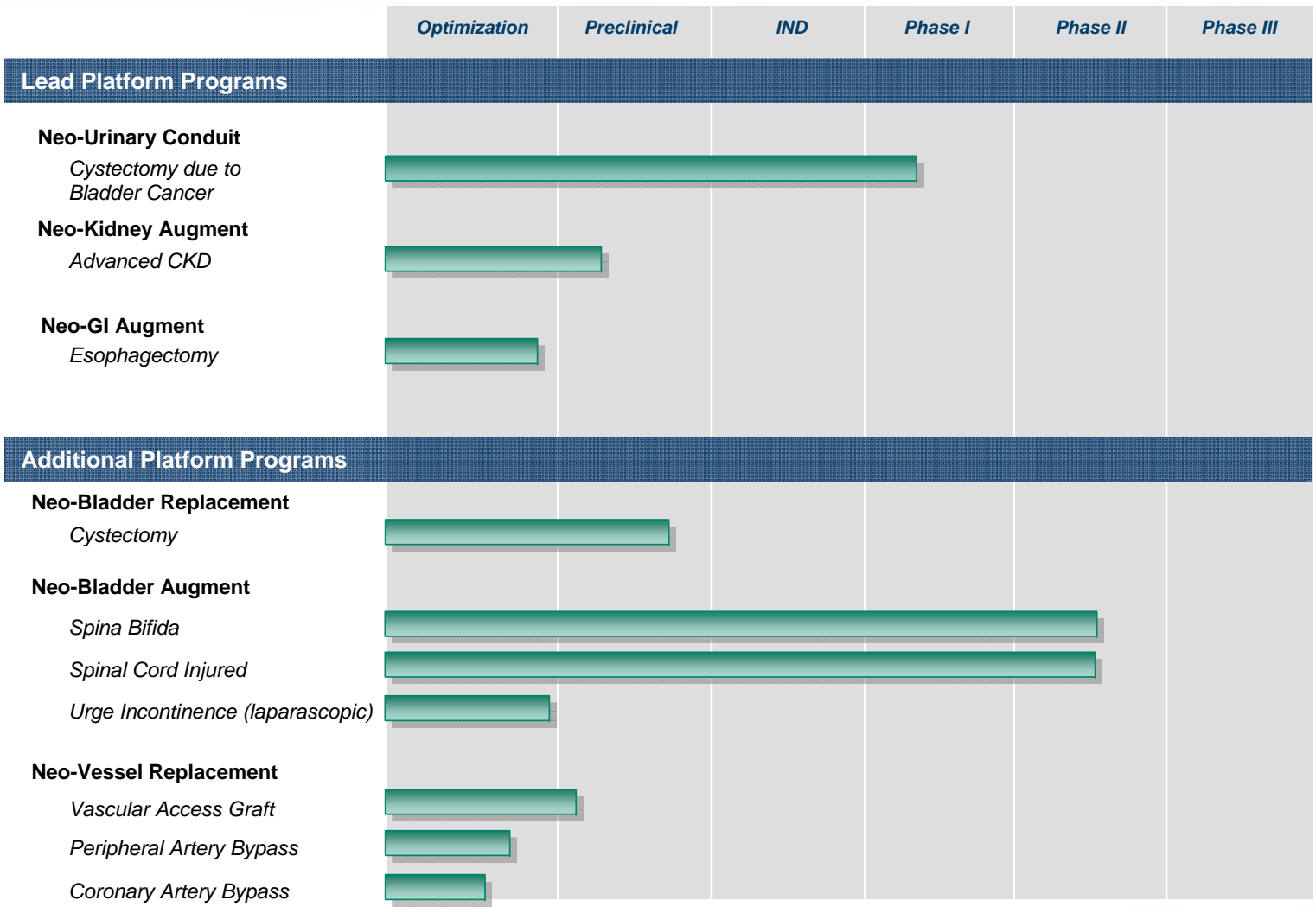
## OUTPUTS

### *Regenerative Templates*



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

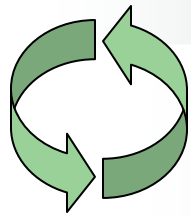
# Tengion Product Pipeline



# Accelerating development timelines for *Clinical Translation of regenerative medicine products*

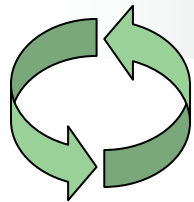
Iterative *in vitro* & *in vivo*  
testing of early-stage  
prototypes

- **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***

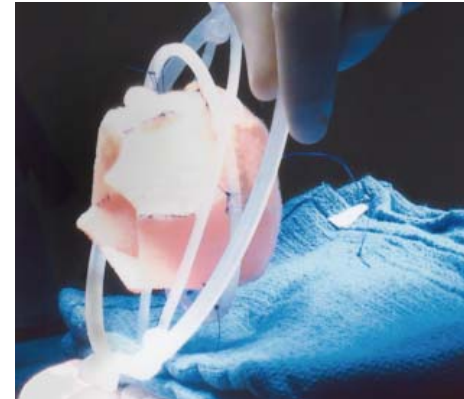
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# Regenerating urinary tissue for unmet needs

## *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**

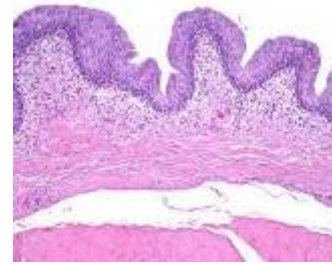
- *Provides exit for urine after bladder removal due to cancer*
- *PLGA scaffold + adipose-derived smooth muscle cells*
- *Regenerates urinary tissue*



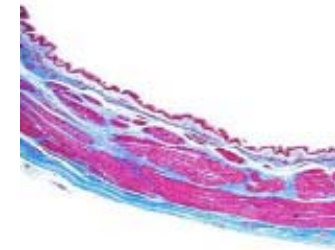
# Neo-Urinary Conduit – Preclinical Data (GLP n=66) *Regeneration with urine flow in a swine model*



**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***

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# Neo-Urinary Conduit

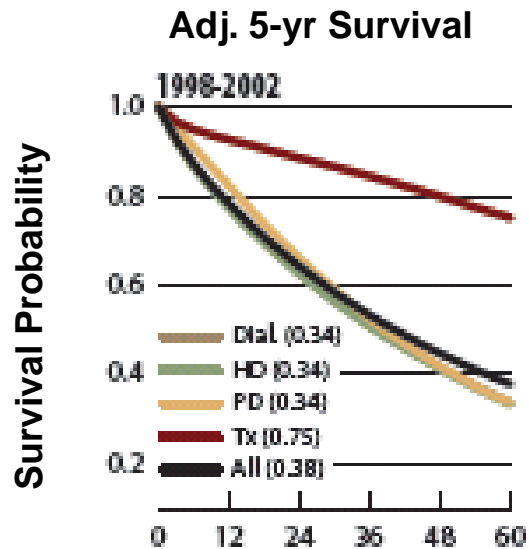
## *Regulatory pathway to approval*

### **FDA**

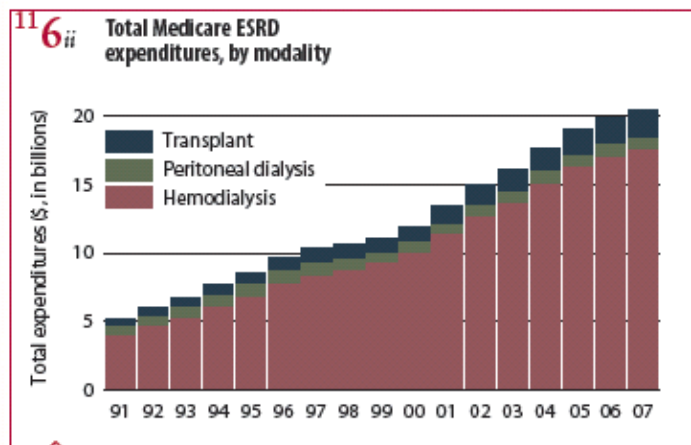
- *BLA pathway, CBER leads and CDRH collaborates*
- *IND approved within 30 days*
- *Frequent interactions with FDA since discovery*
- *Orphan designation may be applicable in the future*
- *US manufacturing facilities may be suitable through commercialization*

# Neo-Kidney Augment™ (NKA)

*Chronic Renal Failure is a leading cause of death worldwide*



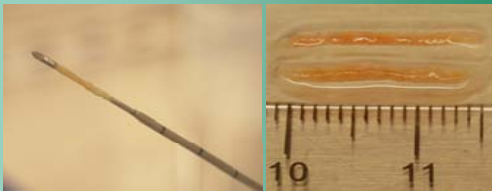
- **>350,000 people with end-stage renal disease (ESRD)**
- **>50,000 people with ESRD are waiting for kidney transplants in the US**
- **>100,000 people start dialysis annually in the US**
  - \$60,000 1<sup>st</sup> year cost
  - \$22 billion in Medicare direct costs annually
- **New treatment modalities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



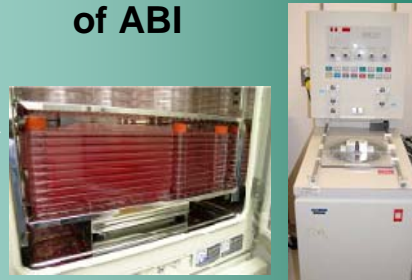
# Neo-Kidney Augment™ (NKA)

*Applying Tengion's regenerative platform to a solid organ*

Bioactive Renal Cells from  
Kidney Biopsy



Isolation / Expansion  
of ABI



Bioreactor System for  
NKA Production\*



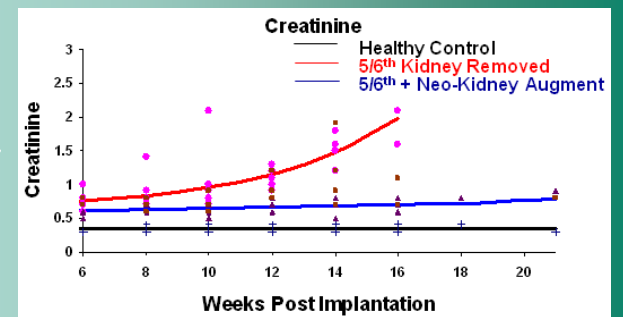
Injectable Delivery System\*



*In vivo* Delivery



Functional Regeneration\*\*



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

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

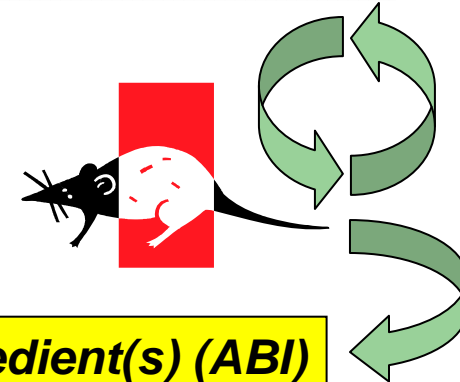
*Generate testable array of 'kidney components' based on native tissue composition*



*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*

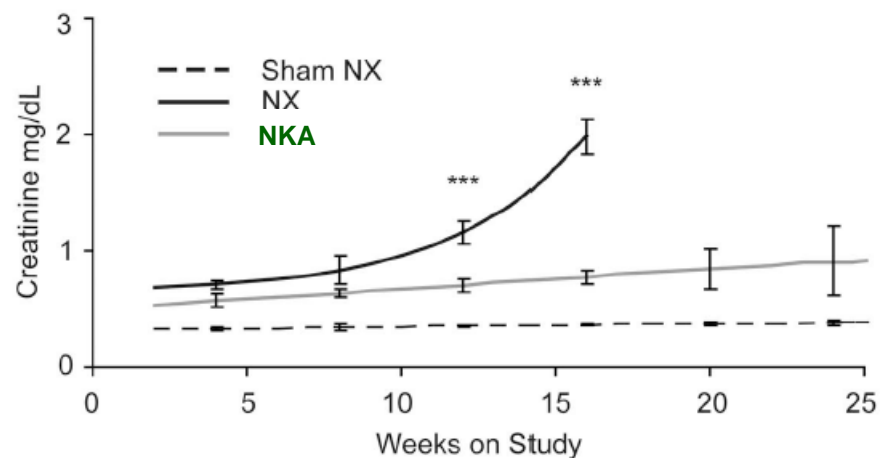
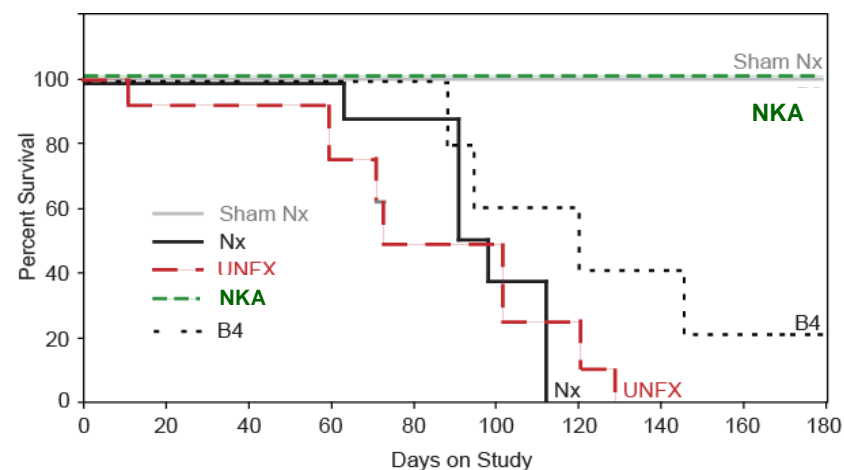


**Identification of Active Biologic Ingredient(s) (ABI)**

# 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



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# NKA provides structural and functional regeneration

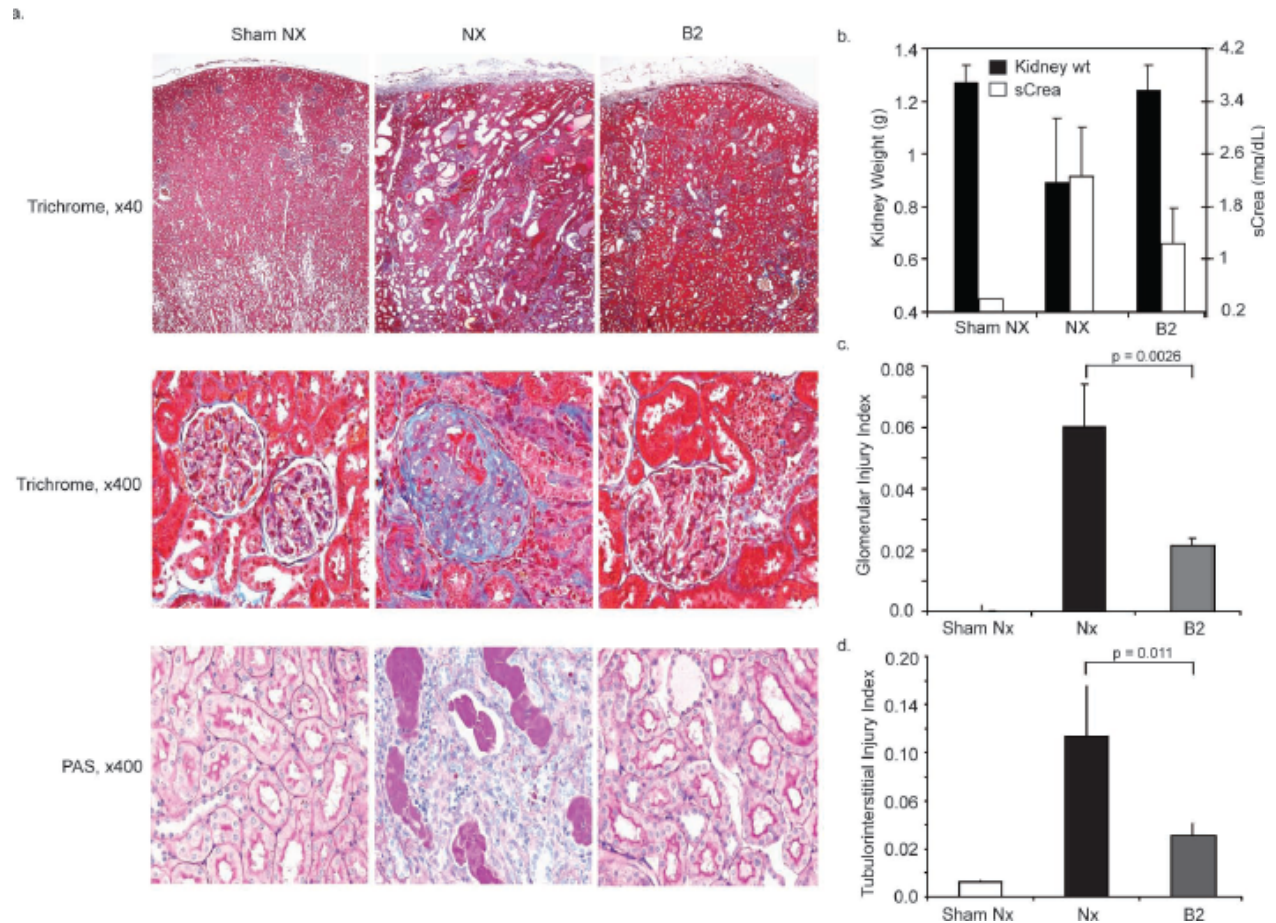
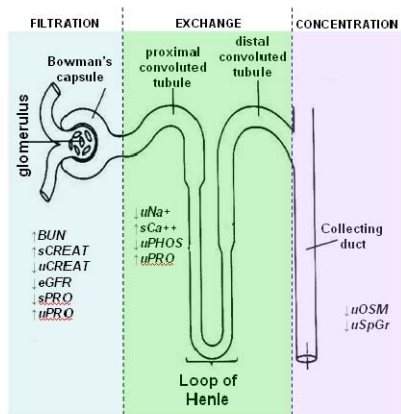
## Systemic endpoints correlate with durable tissue-level improvements

### Functional regeneration

- Glomeruli
- Tubules

### Reduced fibrosis

- Glomerular
- Tubulointerstitial



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

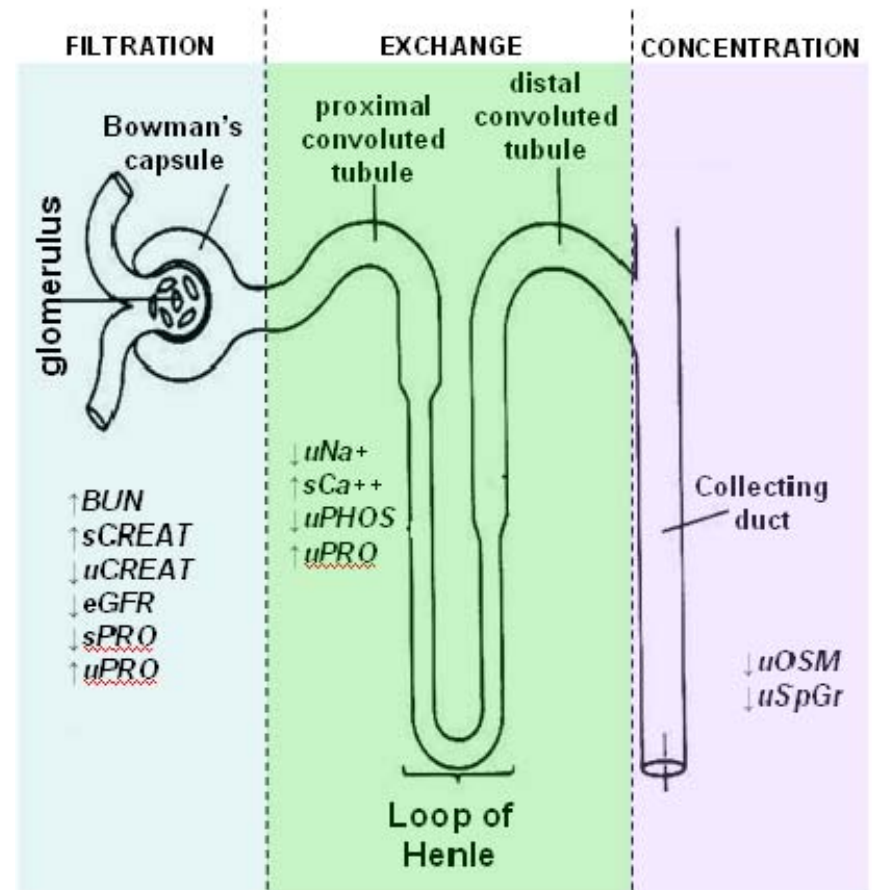
- ***NKA ABI validated in 5/6 Nx rodent model of CKD due to renal mass insufficiency\****
  - *Robust therapeutic effect*
  - *Reproducible across independent studies*
- ***Will the NKA ABI function in a model of CKD secondary to obesity and Type 2 Diabetes?***
  - *Active investigation of NKA ABI in 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*

# Obese ZSF1 rats model progressive nephropathy

## Renal disease secondary to diabetes mellitus and hypertension

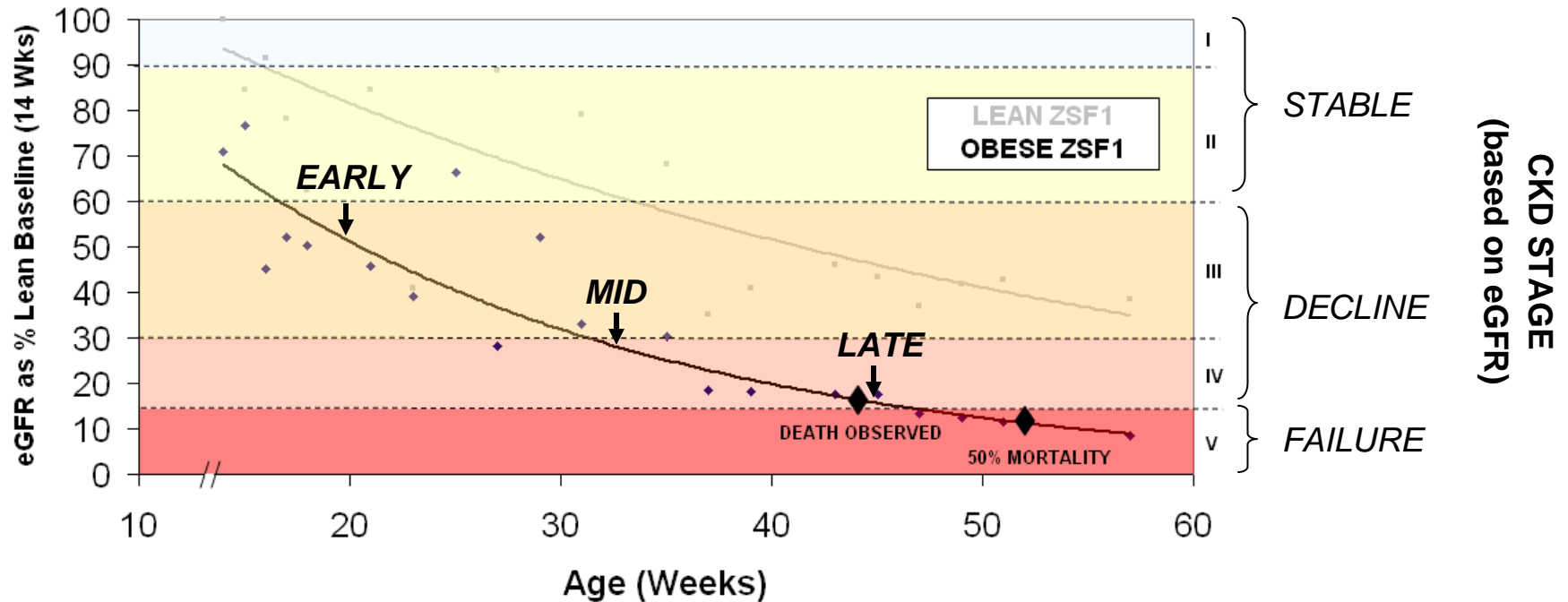
### Aggressive Metabolic Disease

- ~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



# 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*

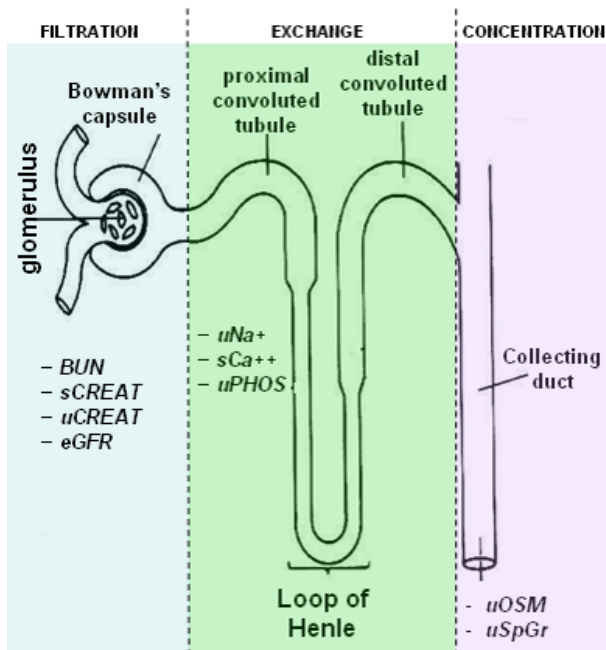
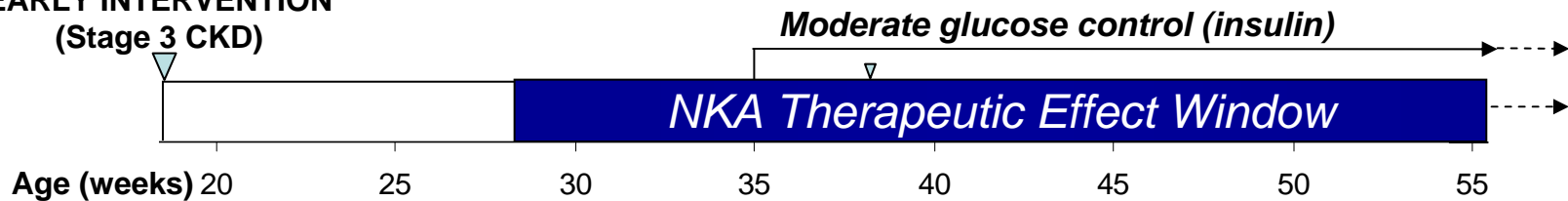
### *Intervention strategies:*

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

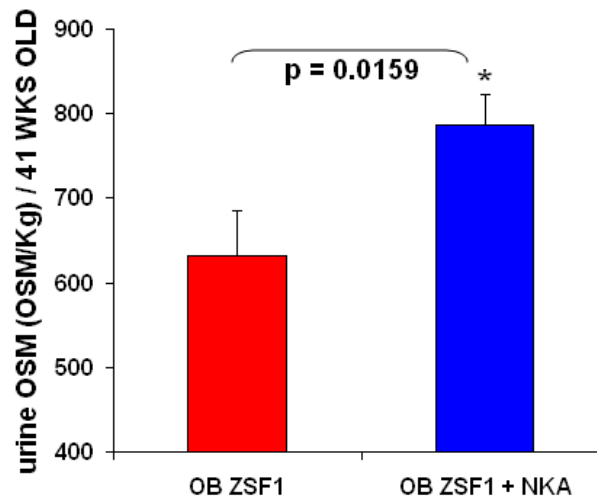
# NKA ABI improved function throughout the nephron

## Collecting ducts, tubules, and glomeruli

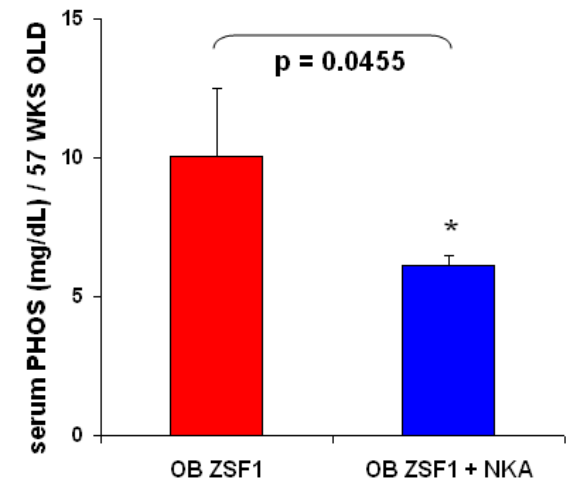
EARLY INTERVENTION  
(Stage 3 CKD)



**CONCENTRATION**  
(uOSM)

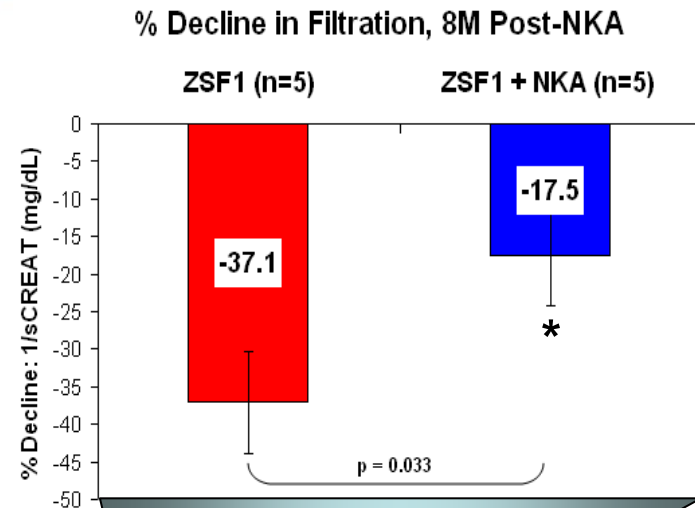
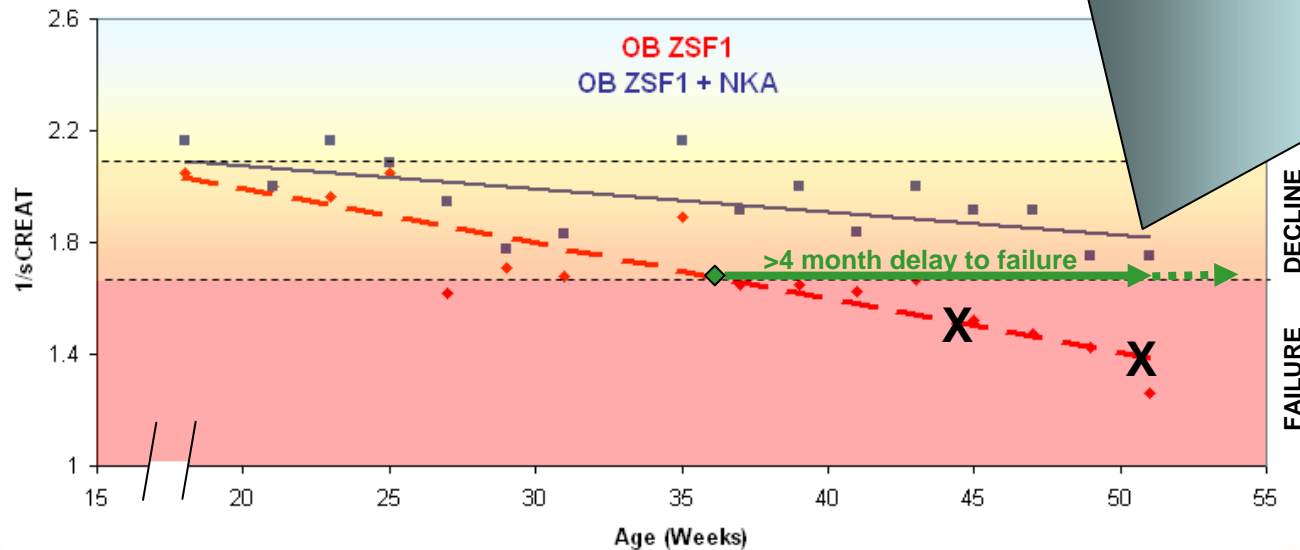


**EXCHANGE**  
(PHOS)



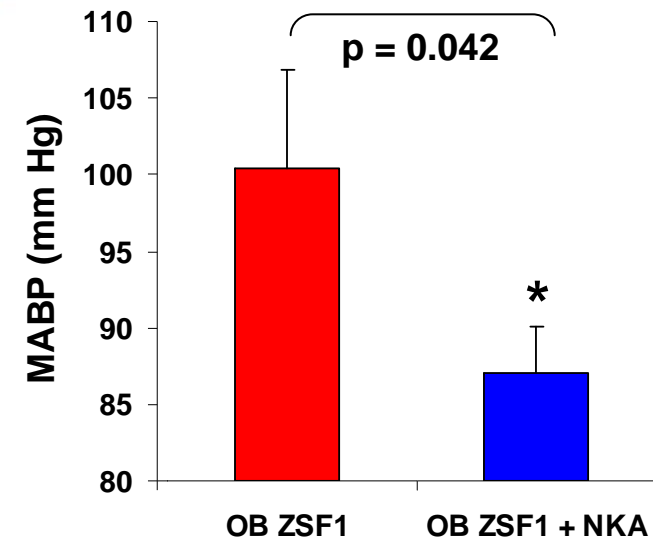
# NKA ABI preserved renal filtration function For up to 8 mo post-treatment (ZSF-1)

- **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*

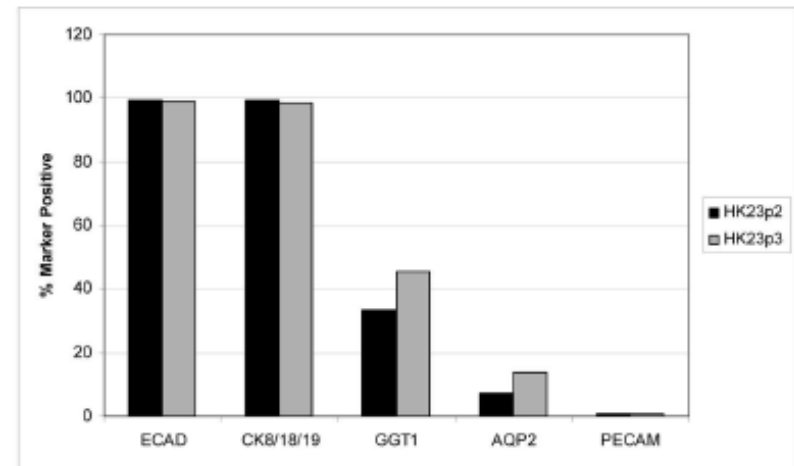
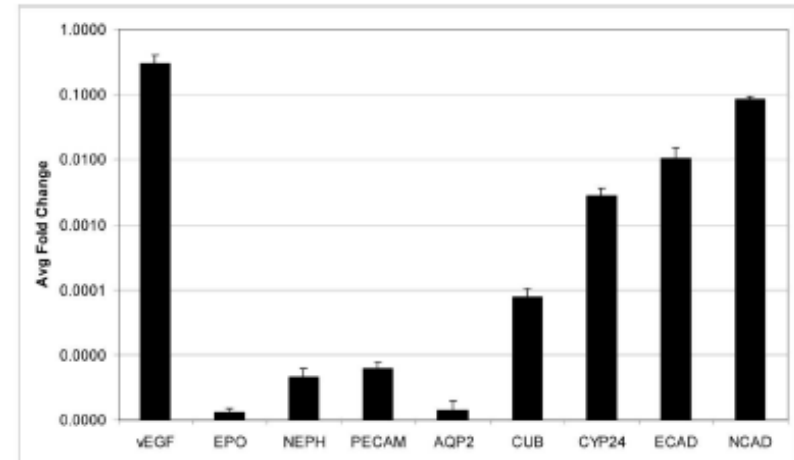
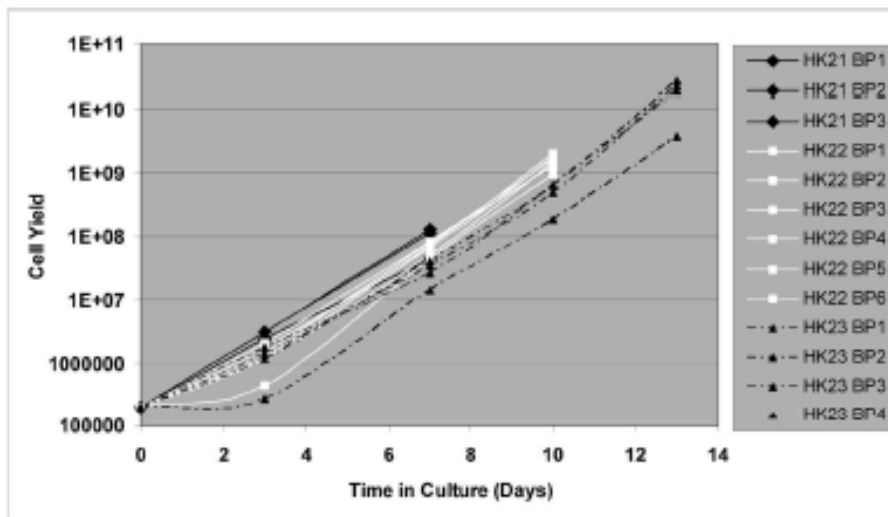


<i>Treatment Group</i>	<i>57-week Survival</i>
<b>OB ZSF1</b>	<b>40% (2/5)</b>
<b>OB ZSF1 + NKA ABI</b>	<b>100% (5/5)</b>

# 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**



# Development of NKA product candidate

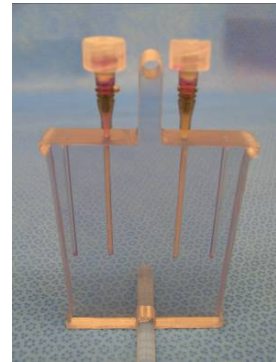
## To target delivery, increase stability, and expand use

### Product Candidate

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

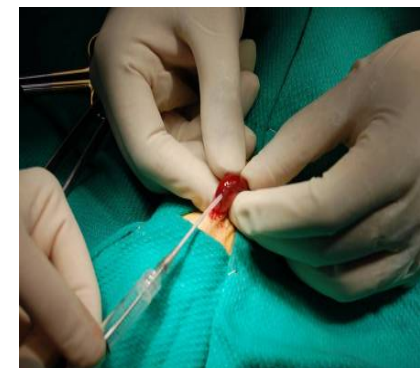
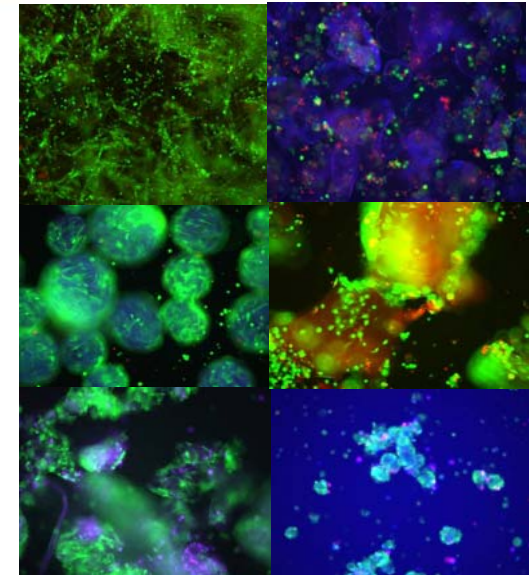
### Delivery System

- Bioreactor system for stable transport and delivery of product



### Clinical Testing – Surgical Options

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



# 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*

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