UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): August 21, 2023

Eloxx Pharmaceuticals, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-31326**	**84-1368850**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

480 Arsenal Way, Suite 130, Watertown, MA	**02451**
(Address of principal executive offices)	**(Zip Code)**

(Registrant's telephone number, including area code): (781) 577-5300

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.01 par value per share	ELOX	The Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On August 21, 2023, Eloxx Pharmaceuticals, Inc. (the "Company") posted an updated corporate presentation within the "Investors" section of the Company's website, which is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Item 7.01 of this Current Report on Form 8-K (including Exhibit 99.1 hereto) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that Section, nor shall it be deemed to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Presentation of Eloxx Pharmaceuticals, Inc., dated August 21, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: August 21, 2023

ELOXX PHARMACEUTICALS, INC.

By: /s/ Sumit Aggarwal
Name: Sumit Aggarwal
Title: President and Chief Executive Officer

Exhibit 99.1

RARE Thinking for RARE Solutions

Small Molecule Gene Therapy

August 2023

Forward-looking statements

This presentation contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words *"expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook"* and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, including: the development of the Company's readthrough technology; the approval of the Company's patent applications; the Company's ability to successfully defend its intellectual property or obtain necessary licenses at a cost acceptable to the Company, if at all; the successful implementation of the Company's research and development programs and collaborations; the Company's ability to obtain applicable regulatory approvals for its current and future product candidates; the acceptance by the market of the Company's products should they receive regulatory approval; the timing and success of the Company's preliminary studies, preclinical research, clinical trials, and related regulatory filings; the ability of the Company to consummate additional financings as needed; the impact of global health concerns, such as the COVID-19 global pandemic, on our ability to continue our clinical and preclinical programs and otherwise operate our business effectively; including successfully integrating the combined companies; as well as those discussed in more detail in our Annual Report on Form 10-K and our other reports filed with the Securities and Exchange Commission.

Clinical stage small molecule gene therapy biopharma poised for value creation

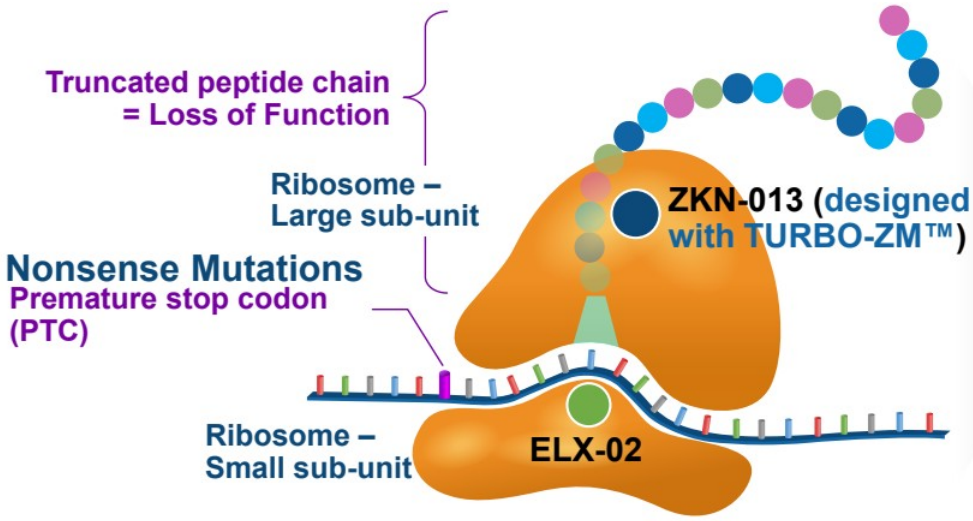
Small molecule **genetic therapies** for nonsense mutations proven to restore full-length proteins

ELX-02: Ready for **Alport Syndrome pivotal study** with **biopsy confirmed disease regression.** Preclinical POC in **ADPKD***

ZKN-013: Oral agent ready for **Phase 1** start; robust preclinical efficacy in **RDEB** and **FAP. Potential in ADPKD****

Two clinical stage drugs designed to treat inherited diseases with nonsense mutations

Nonsense mutation overview and MOA of Eloxx therapies

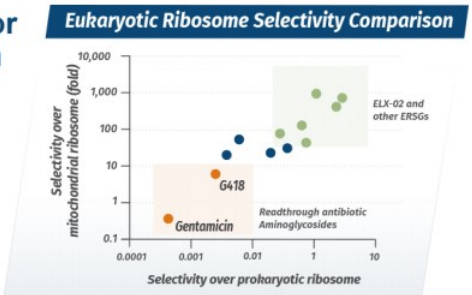


Clinical leads ELX-02 and ZKN-013 have demonstrated superior functional protein restoration

Lead drugs designed for superior efficacy than proven readthrough antibiotics

1 Designer aminoglycosides: Eukaryotic ribosome selective glycosides (ERSGs)

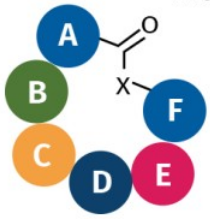
ERSGs designed for nonsense mutation readthrough[1]



- **ELX-02** has **demonstrated clinical efficacy** in **Alport syndrome** and activity in CF
- Up to **1,000-fold more selective** than Gentamicin
- Minimal to **no antibiotic** activity
- Suitable chronic delivery

2 Designer macrolides: Ribosome modulating agents (RMAs)

TURBO-ZM™ (TUning the RiBOsome with Zikani Molecules



A Modulate
- Phamacokinetics
- Safety: cardiac, liver
- Oral bioavailability

B Optimize for
- Readthrough
- Protein translation inhibition

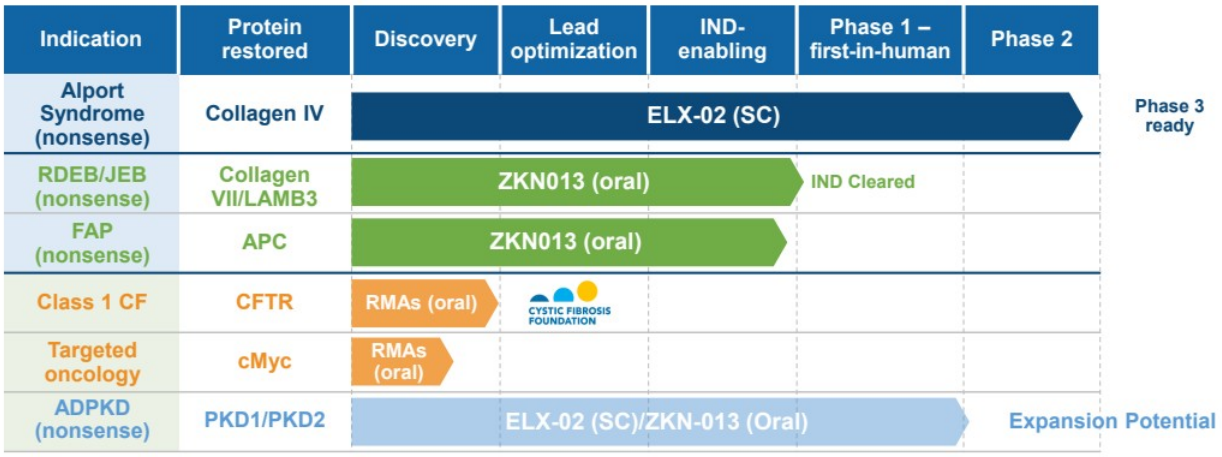
D Essential for ribosomal binding

E Modulate cytoplasm and mitochondrial ribosome-binding activity

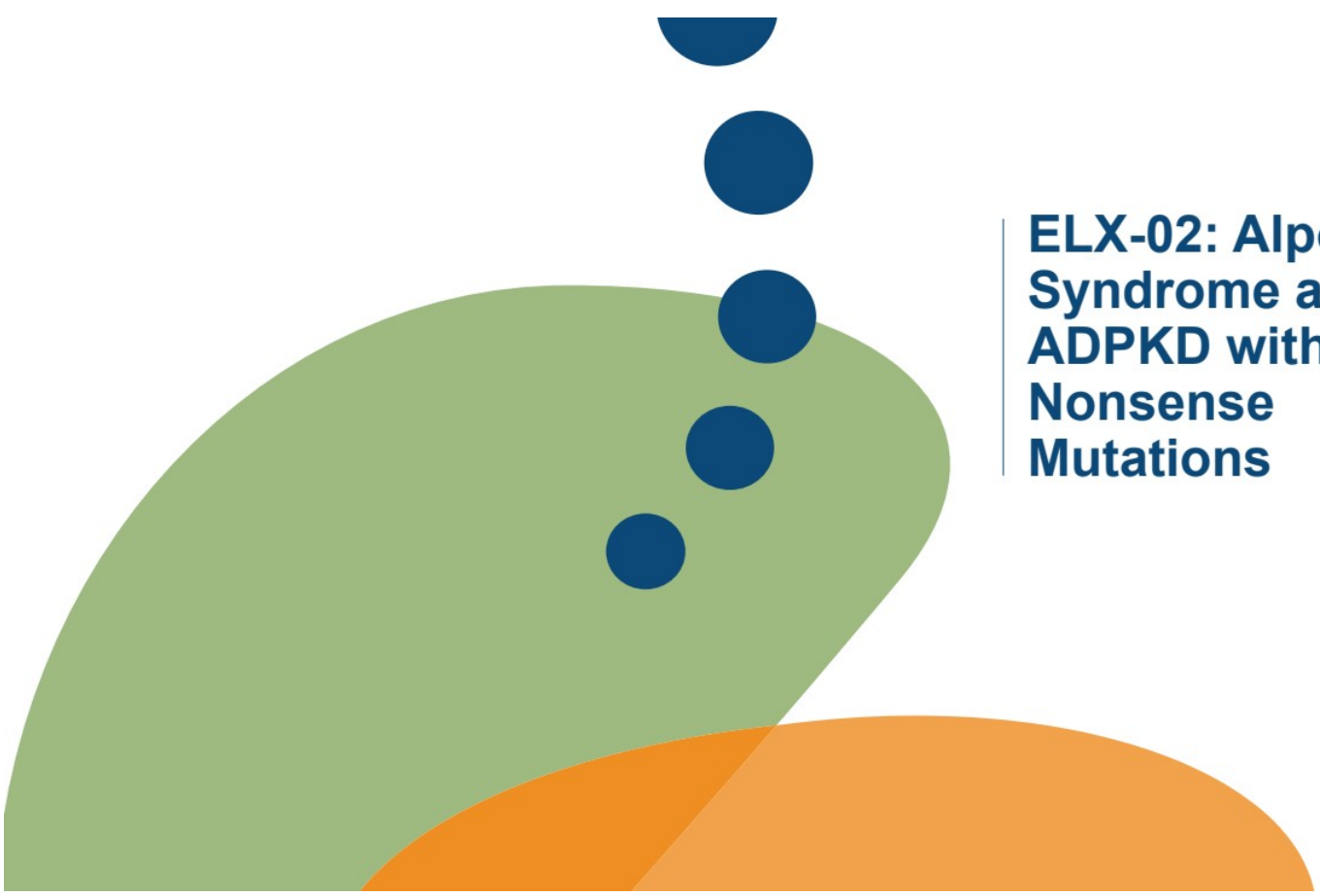
- Library of **>2,000 RMAs** including **ZKN-013**
- Stronger human ribosome binding affinity; **minimal antibiotic** activity
- **Oral**, well-tolerated and **smaller** than macrolide antibiotics

[1]Data adapted from: *J Med Chem*. 2012 Dec 13;55(23):10630-43.1;

Pipeline of potential first-in-class therapies to treat rare kidney and orphan diseases



Class 1 CF: Cystic fibrosis patients with class1 mutations; **RDEB/JEB:** Recessive Dystrophic/Junctional Epidermolysis Bullosa; **FAP**: Familial adenomatous polyposis; **PoC**: Proof of concept; SC: Subcutaneous; **IND**: Investigational New Drug



ELX-02: Alport Syndrome and ADPKD with Nonsense Mutations

ELX-02 has shown robust preclinical and clinical protein restoration across multiple indications

Summary of ELX-02 nonsense mutation readthrough activity

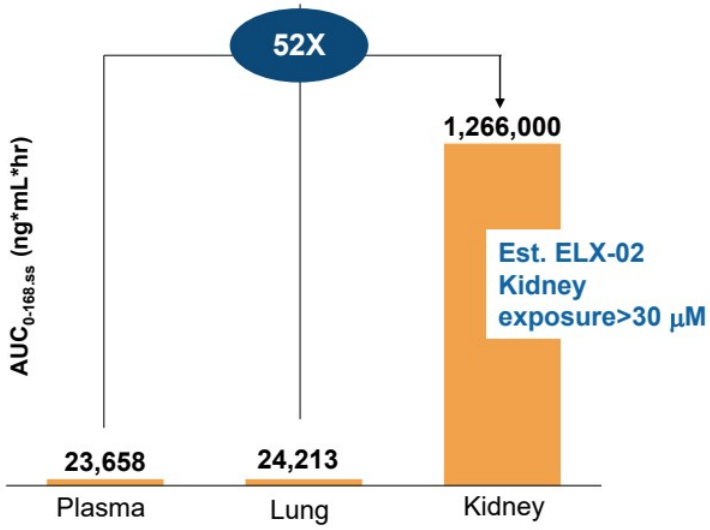
Disease	*In vitro*	*In vivo*	Organoids or Primary patient cells	Patients
Cystic fibrosis	✓	✓	✓	✓
Cystinosis	✓	✓	✓	✓
Alport syndrome	✓			✓
ADPKD	✓		✓	
RDEB	✓		✓	
JEB	✓		✓	
DMD	✓	✓		
MPS	✓	✓		
Rett syndrome	✓	✓		
Inherited retinal disorders	✓	✓		

Rare kid diseases

ADPKD: Autosomal dominant polycystic kidney disease; **RDEB:** Recessive Dystrophic Epidermolysis Bullosa; **JEB:** Junctional Epidermolysis Bullosa; **DMD:** Duchenne muscular dystrophy; **MPS:** Mucopolysaccharidosis

ELX-02 well suited to treat rare renal diseases

Estimated human exposure in Plasma, Lung and Kidney at 1 mg/kg



- **ELX-02 like other aminoglycosides (e.g., Gentamicin) binds to LRP2 protein Megalin**
- **Megalin is found in the glomerulus and proximal tubules in the kidney, the inner ear and eye**

Estimation based on allometric scaling of mouse, rat and dog plasma and kidney data PLUS plasma PK from SAD and MAD studies
Source: d1pbpk\pbpk\cognigen\2018-01-30-pbpk-elx02-refined-simulation\listing-ratio-auc168ss-human-bytissue.rtf.

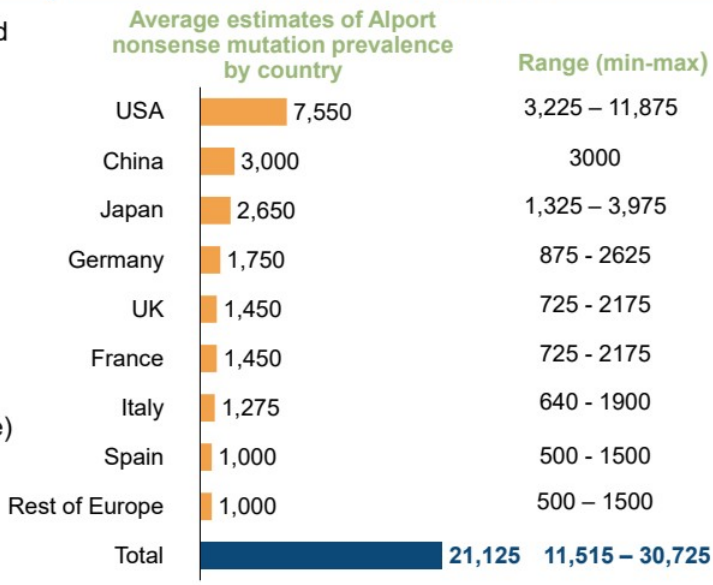
Alport syndrome: rare glomerular kidney disease caused by mutations in Col4 gene

Alport syndrome nonsense mutation disease overview

Alport disease overview[1,2]

- **Inherited glomerular kidney disease** caused by **defect in Col4 gene**
  - X-linked in 85% - Col4A5 gene
  - Recessive in ~15% - Col4A3/4 genes
- **Nonsense mutations result in truncated proteins resulting in worse outcomes**
  - **Over 70 nonsense mutations** in Alport described
- **No approved therapies**
  - **Limited therapeutic options** (RAAS Blockade)

Global estimated Alport nonsense mutation prevalence[3]



[1]J Am Soc Nephrolv.28(6); 2017 JunPMC5461786
[2]J Clin Invest 1995 Sep;96(3):1404-13
[3]JASN 32(9):p 2273-2290, September 2021.

Glomerular and podocyte injury leads to proteinuria and hematuria resulting in loss of kidney function

Alport syndrome disease progression and clinical manifestation

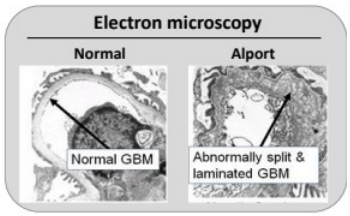
Disease Pathogenesis

Progressive podocyte damage/loss of basement membrane from *COL4A3*, *A4* or *A5* mutations

Podocyte foot process effacement (loss) leads to leakage of red cells and protein into urine

Progressive damage and fibrosis

Clinical manifestation



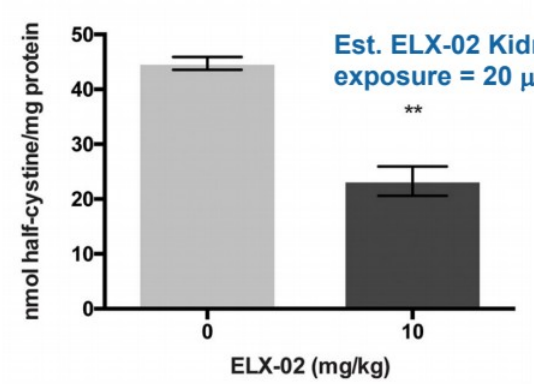
Hematuria and proteinuria

eGFR loss leading to kidney failure

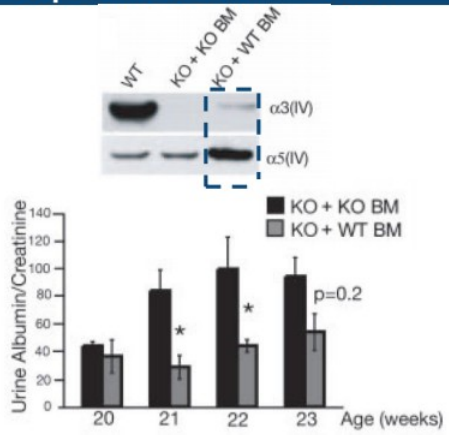
Preclinical mouse studies support ELX-02 activity in kidney and Alport

Preclinical studies in Cystinosis (ELX-02) and Alport (COL4A3 replacement)

Kidney cystine levels in CTNSY226X/Y226X mice after 3-week ELX-02 treatment[1]



COL IV A3 bone marrow treatment of C57BL/6 Alport mice over 3 weeks[2]

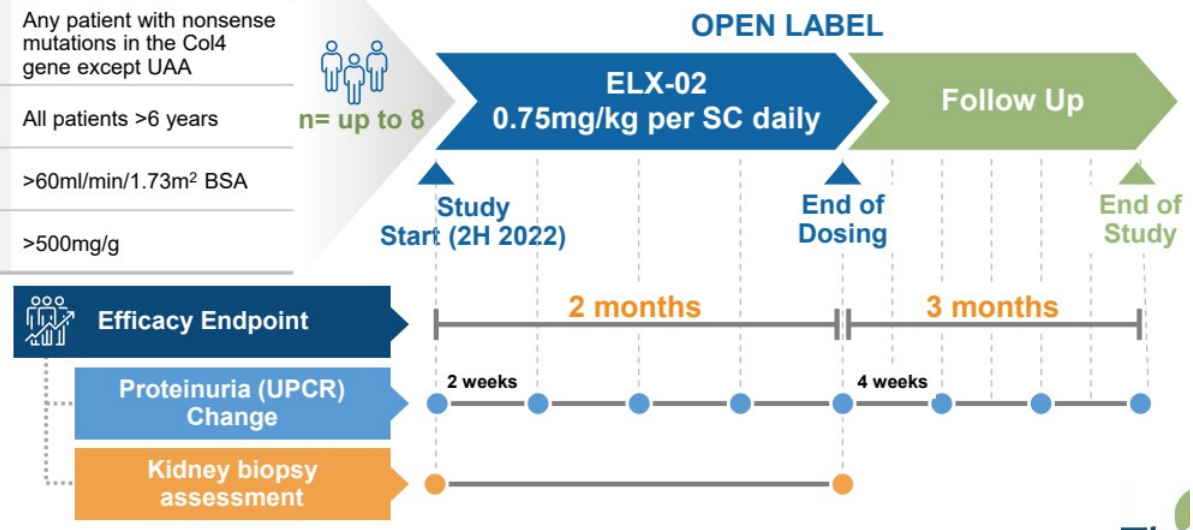


[1]PLoS One 2019 Dec 4;14(12); Bi-weekly treatment with ELX-02 of Cystinosis mouse with nonsense mutation

2 JASN November 2009, 20 (11) 2359-2370. Wild type (WT) Bi-weekly COL4A3 +/- bone marrow (BM) treatment in C57BL/6 knockout mice aged 20 weeks over 3 weeks. treated mice: n=4; Knockout untreated mice: n=3 (*p<0.05)

Alport Phase 2 POC trial designed to show evidence for proteinuria reduction and disease regression

Inclusion Parameters	Criteria
Genotype	Any patient with nonsense mutations in the Col4 gene except UAA
Age	All patients >6 years
eGFR	>60ml/min/1.73m^2 BSA
Proteinuria	>500mg/g



Proteinuria remission rate likely approvable endpoint reflecting glomerular repair in Alport

Definition of remission and rationale

Efficacy end point	Rationale for likely approval endpoint
Remission rate: Number of patients in remission defined as: • >=50% UPCR decline, or • UPCR<=300mg/g	**Spontaneous remission not possible in this genetic disease** • Proteinuria remission is well accepted in renal glomeruli diseases • Reduction correlates with improvement in kidney function in glomerular diseases • Drugs in lupus nephritis approved with a remission rate as low as a 1 in 10 patients

"FDA has already accepted [for a number of primary glomerular diseases] complete remission" or near-"normalization" of proteinuria as a surrogate end point and basis for accelerated and/or traditional approval" – *FDA Staff*[1]

[1]AJKD Vol75 Issue1 4-5 January 2020

Phase 2 patients had autosomal recessive disease with differing levels of background RAAS blockade at baseline

Baseline characteristics of patients in Phase 2

Patient	Age	Sex	COl4 Gene Affected	Nonsense Mutation	RAAS Block dose	Cr (mg/dL)	Proteinuria (mg/g)
4401-01	13	Male	COL4A4	**c.2906C>G*; p.Ser969X**	Enalapril 2.5 mg QD	0.7	1299
4401-02	13	Male	COL4A4	**c.2906C>G*; p.Ser969X**	Enalapril 32.5 mg QD	0.5	1646
4402-01	19	Female	COL4A4	**c.2906C>G*; p.Ser969X**	Enalapril 5 mg QD	1.31	1645

RaDaR National Registry of Rare Kidney Diseases

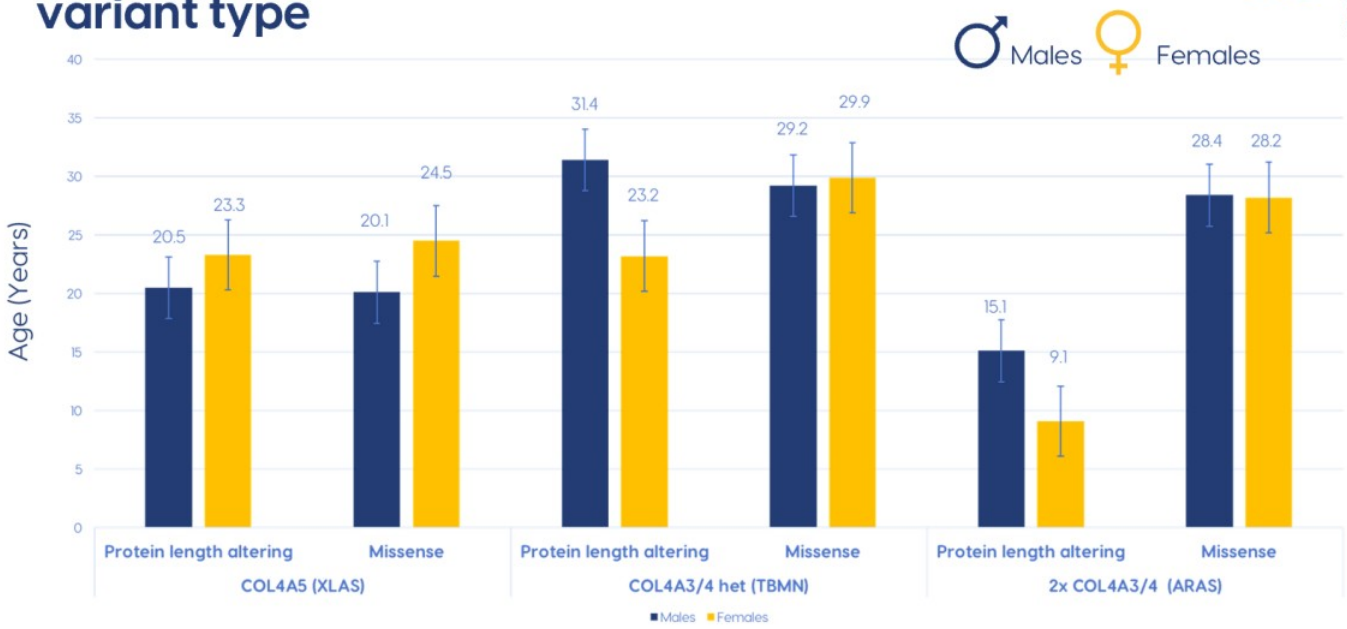
UKKA UK Kidney Association

Data from RaDaR natural history study indicates that Alport syndrome **patients with autosomal recessive COL4A4 mutations** have **severest disease** with **more rapid progression to kidney failure**

*Most common mutation in the UK

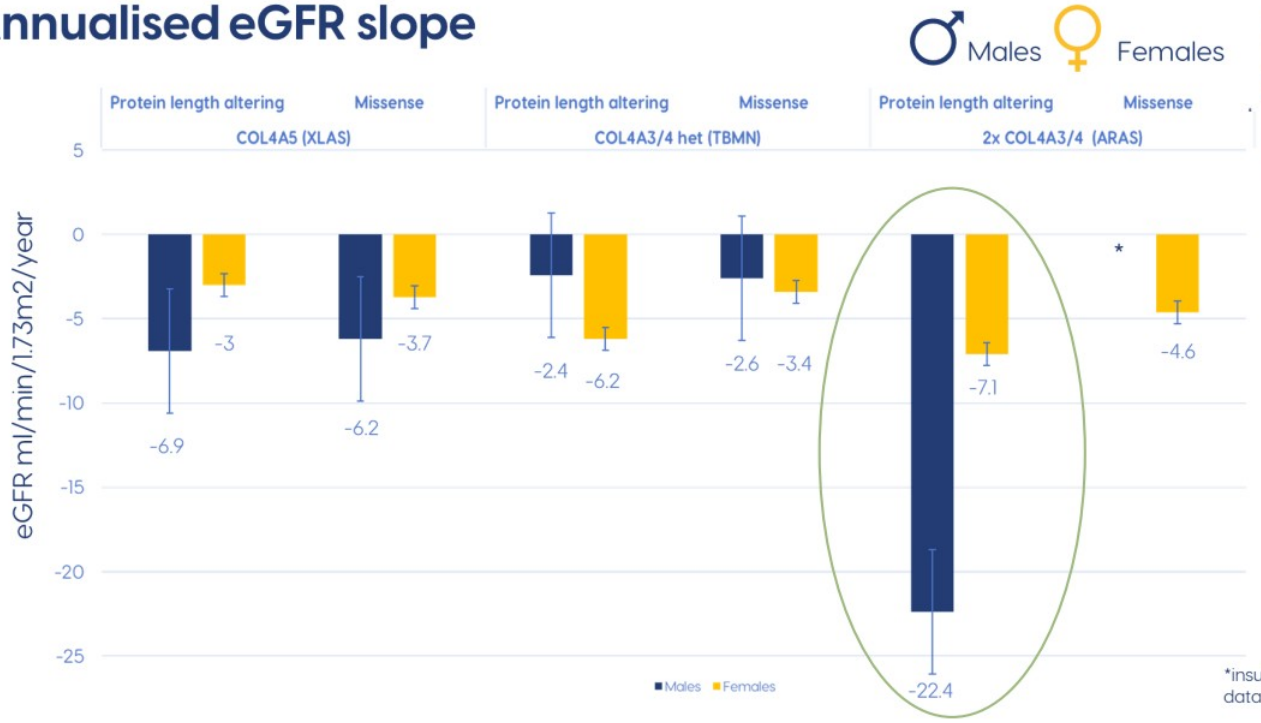
Alport patient ages in trial consistent with data from RaDaR registry for those with truncated COL IV A4 proteins

Median age at diagnosis, by genotype, Sex and variant type



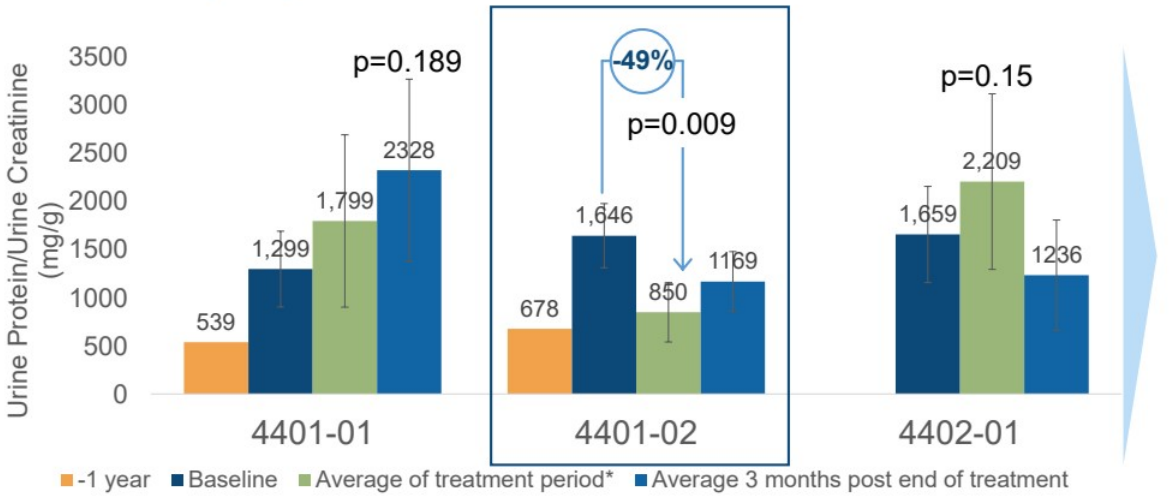
High proteinuria at baseline also consistent with RaDaR data suggesting worst renal outcomes

Annualised eGFR slope



Proteinuria remission confirmed in one Alport patient

Phase 2 Alport patient results



Patient 4401-02 achieved remissi after completing weeks of treatme

- 5 out of 8 UPCR readings were o average 53% below baseline
- UPCR values rebounded after end of treatmen in responder

* UPCR averaged over 6 values collected in 8 weeks for 4401-01 and 4401-02. UPCR values collected for 4401-01 and 4401-02 at week 6 were excluded as they were deemed to be unreliable due to inconsistent processing during Easter holidays and inconsistency with the clinical presentation. All 8 UPCR values included for 4401-02

All patients had biopsy confirmed disease regression suggesting clinical efficacy with longer treatment duration

Transmission electron microscopy (TEM) assessment of podocyte foot process effacement in kidney biopsies of all patients in Phase 2 trial

Patient	Pre-treatment podocyte foot process effacement	Post-treatment podocyte foot process effacement
4401-01	Widespread foot process effacement present	Segmental foot process effacement present
4401-02 (Patient achieved remission)	Widespread foot process effacement present	Segmental foot process effacement present
4402-01	Moderate to severe foot process effacement present	Moderate segmental foot process effacement present

"As a physician scientist with a longtime focus on podocytes, I find these electron microscopy results compelling since the demonstrated improvement in podocyte foot process effacement shows that ELX-02 has substantial potential to treat Alport syndrome," - Dr. Peter Mundel, renowned expert in kidney diseases)

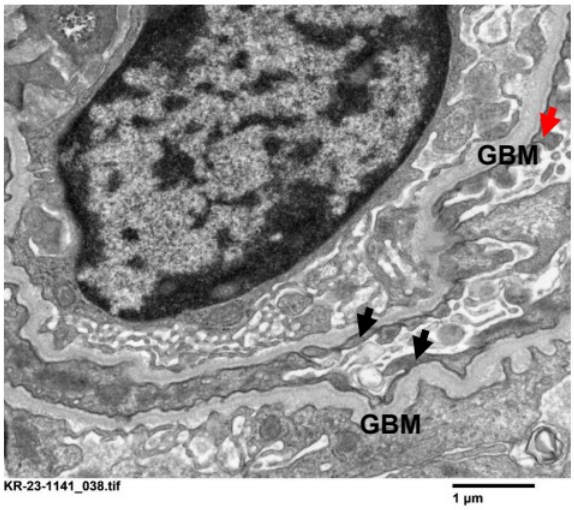
Responder biopsies shows disease regression with improvement in podocyte foot process effacement

TEM sample images from kidney biopsies of patient 4401-02

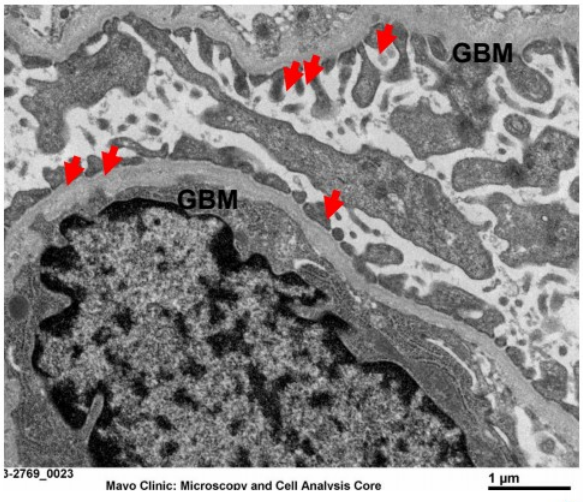
= foot process

= effaced foot pr

Pre-treatment: Widespread podocyte foot process effacement



Post-treatment (Day 60): Segmental podocyte foot process effacement



TEM images and analysis done at Mayo Clinic by kidney pathologist on a blinded basis

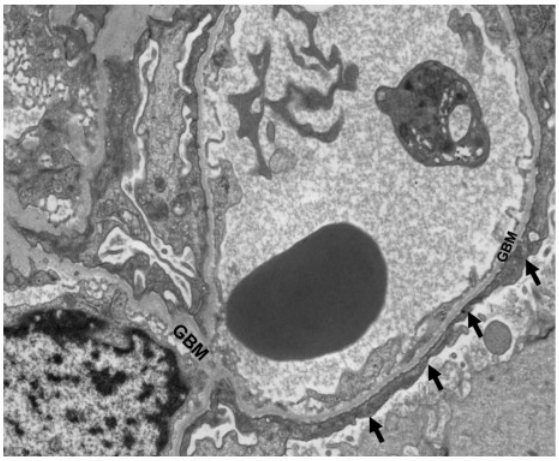
Improvement in podocyte foot process effacement confirms disease regression in non-responder

TEM sample images from kidney biopsies from patient 4401-01

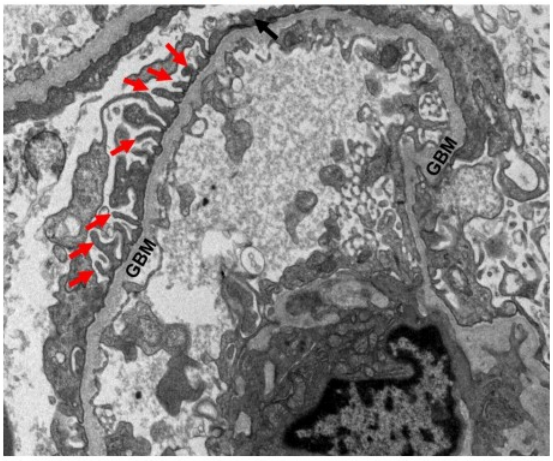
= foot process

= effaced foot pr

Pre-treatment: Widespread podocyte foot process effacement



Post-treatment (Day 60): Segmental podocyte foot process effacement



TEM images and analysis done at Mayo Clinic by kidney pathologist on a blinded basis

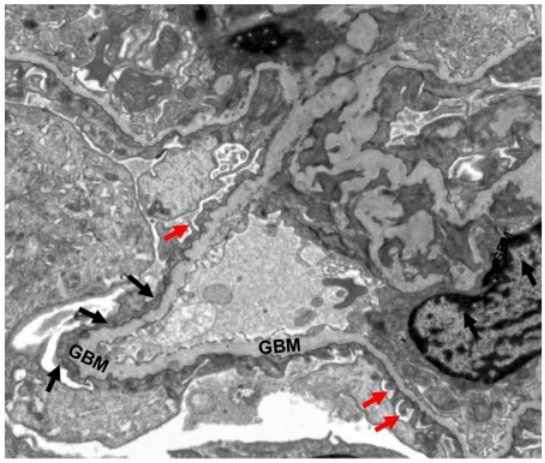
Improvement in podocyte foot process effacement confirms disease regression in non-responder

TEM sample images from kidney biopsies from patient 4402-01

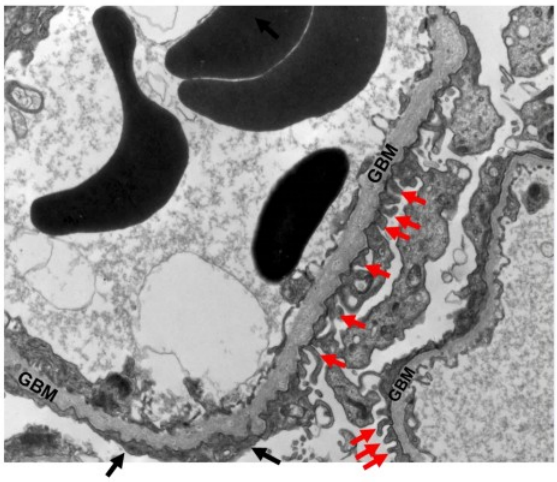
= foot process

= effaced foot pr

Pre-treatment: Widespread podocyte foot process effacement



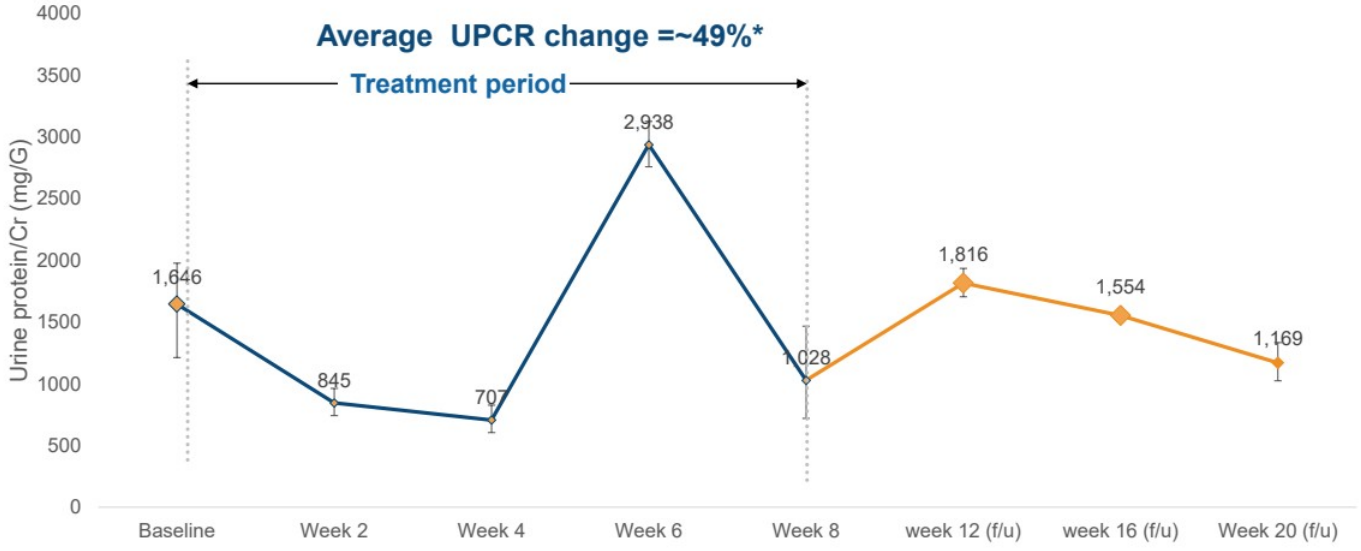
Post-treatment (Day 60): Segmental podocyte foot process effacement



TEM images and analysis done at Mayo Clinic by kidney pathologist on a blinded basis

Rapid remission in Patient 4401-02 with rebound after end of treatment supports drug efficacy

Proteinuria (UPCR) change in patient 4401-02



* UPCR averaged over 6 values collected in 8 weeks. UPCR values collected at week 6 were excluded as they were deemed to be unreliable due to inconsistent processing during Easter holidays and inconsistency with the clinical presentation

Robust safety experience for advancing to longer treatment duration in pivotal study

Cumulative ELX-02 safety experience across all clinical studies

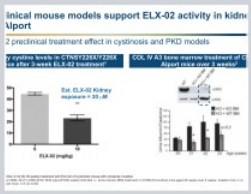
No ELX-02 related SAEs in Phase 1 and 2 studies at doses up to 7.5 mg/kg in 148 subjects with no nephrotoxicity

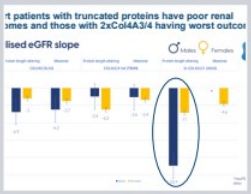
ELX-02 was well tolerated up to 1.5 mg/kg dose across Phase 2 patients (n=34)

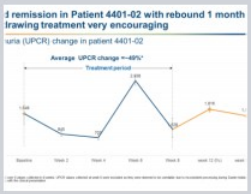
- Combination therapy in CF trials at 1.5 mg/kg showed drug related discontinuations
  - 2 patients discontinued due to injection site reactions (mild to moderate)
  - 1 patient withdrew from trial due to injection burden prior to dosing
  - 1 patient with tinnitus*
- No drug related discontinuations in Alport Phase 2 trial at 0.75mg/kg

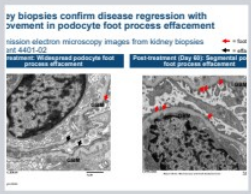
*Patient had an undisclosed history of tinnitus
SAE: Serious adverse events

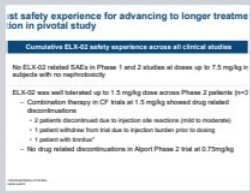
ELX-02 has potential as first gene therapy for Alport patients with nonsense mutations











ELX-02 development in Alport and supported by robust preclinical data

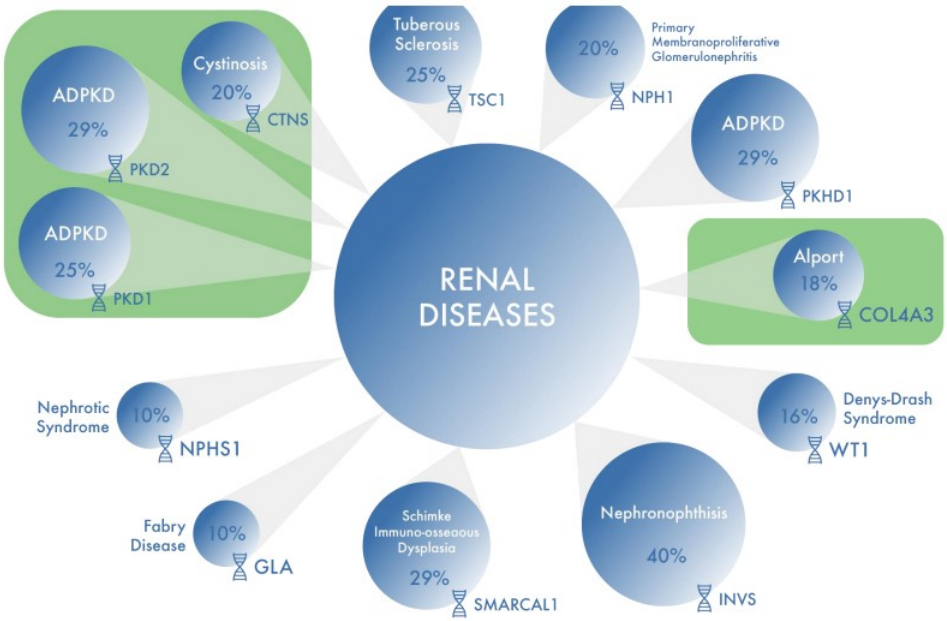
High unmet need in Alport patients with nonsense mutations

Robust clinical effect with 1 out of 3 proteinuria remission rate in Alport study

Biopsy confirmed disease regression with improvement in podocyte foot process effacement in all patients

Robust safety experience supports longer treatment duration

Alport success opens potential for expansion into other renal diseases



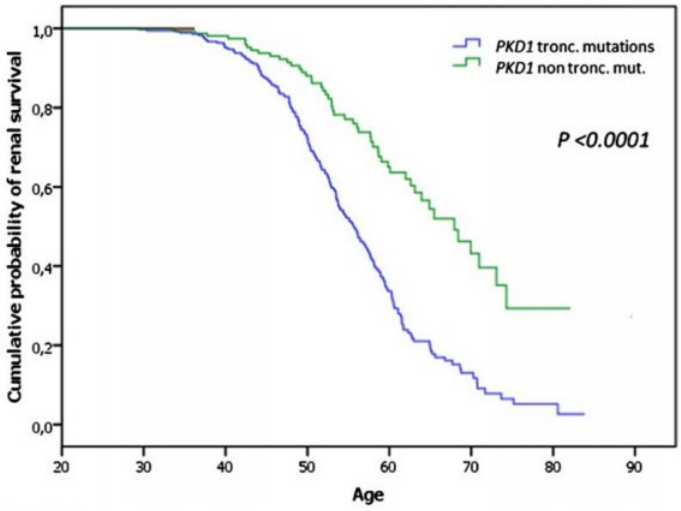
Substantial unmet need remains in multiple renal diseases with high rates of nonsense mutations

Source: Torra et al, UGA hopping: a sport for nephrologists too? *Nephrol Dial Transplant* (2010) 25: 2391–2395

Polycystic kidney disease (ADPKD) attractive disease for nonsense mutation readthrough

Rationale for nonsense readthrough therapy in ADPKD

Relative survival of nonsense vs other PKD1 mutant patients

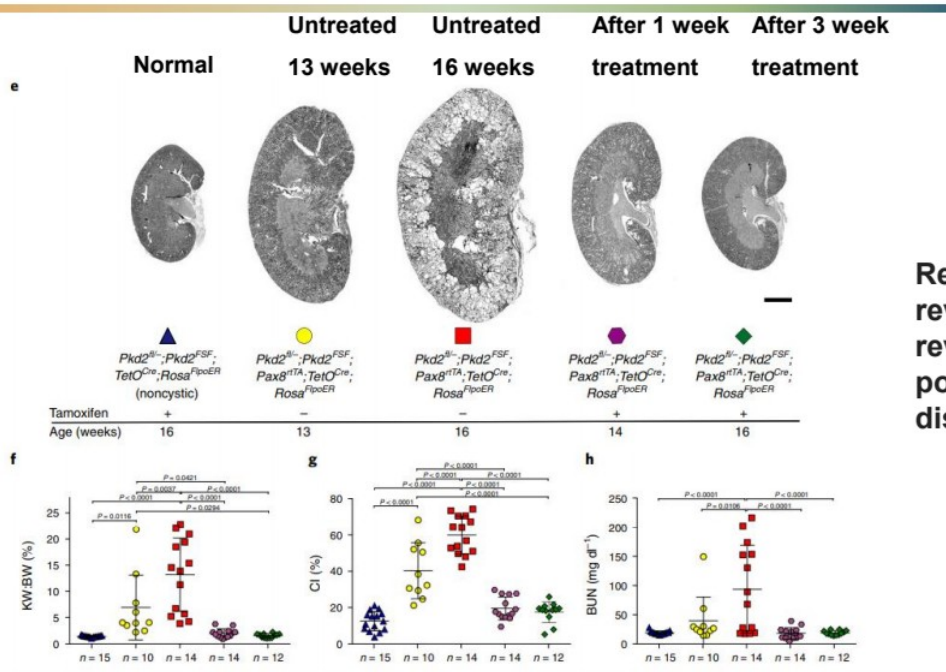


ADPKD disease overview

- **Autosomal Dominant Polycystic Kidney Disease (ADPKD):**
  - Most common genetic kidney disease with >100k patients in US
  - Progressive cystic growth and transformation of kidneys and other organs
  - Renal failure occurring between 40-60y
  - ~1.25M patients in China
- **Nonsense mutant patients have more severe disease**
  - 25-30% of Nonsense mutations in PKD1 and PKD2 genes
  - >75,000 patients in the US alone*
  - 300K nonsense mutation patients estimated in China
- **Available therapy, tolvaptan has significant safety and tolerability issues**

1.Cornec-Le Gall et al. *JASN* 2013
* Based on study by Clearview Partners for Eloxx Pharmaceuticals

Expression of PKD2 reverses cyst formation: Kidney weight, cystic index and BUN



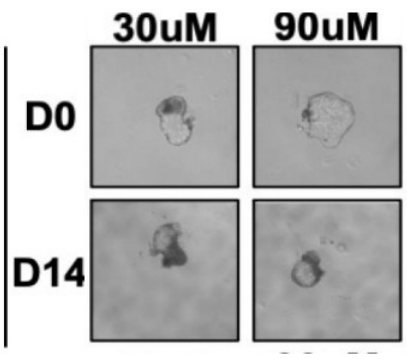
Renal plasticity revealed through reversal of polycystic kidney disease in mice

Ke Dong, , et. A, I Nature Genetic 53, 1649-1663, 2021

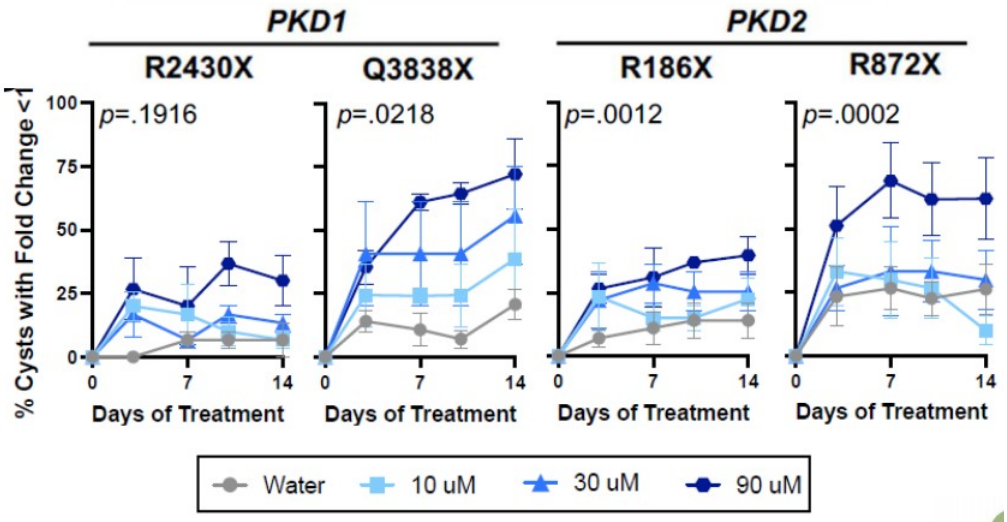
Compelling preclinical data suggests disease regression potential in ADPKD

ELX-02 mediated read-through in nonsense mutant PKD1 and PKD2 organoids*

PKD1 (Q3838X)



Fraction of cysts showing a decrease in size



*Data generated in collaboration with Freedman lab at University of Washington. Single organoids transferred to suspension culture 96-well plates. Treatment is initiated and cyst formation monitored over 14 days.

ZKN-013: RDEB and FAP

ZKN-013 is a potent oral nonsense readthrough drug

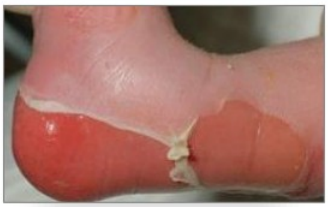
Preclinical activity of ZKN-013

Disease	Gene	Mutations evaluated	Model	Results
Cystic Fibrosis (CF)	CFTR	G542X	ex vivo	**ZKN-013 = ELX-02**
Recessive Dystrophic Epidermolysis bullosa (RDEB)	COL7A1	Q251X, R578X, R613X, R1683X, R2610X	ex vivo	**ZKN-013 > Gentamicin**
Junctional Epidermolysis Bullosa (JEB)	LAMA3	C290X	ex vivo	**ZKN-013 > Gentamicin**
Familial Adenomatous Polyposis (FAP)	APC	L850X R1273X, R1450X	in vivo in vitro	**ZKN-013 : Survival benefit**

RDEB/JEB are rare skin diseases frequently caused by nonsense mutations in the COL7A1 and LAMB3 genes

RDEB and JEB: recessive dystrophic and junctional epidermolysis bullosa

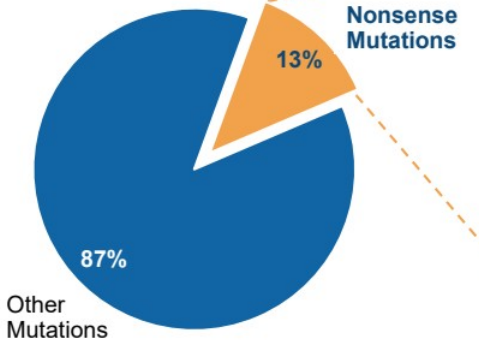
Disease overview



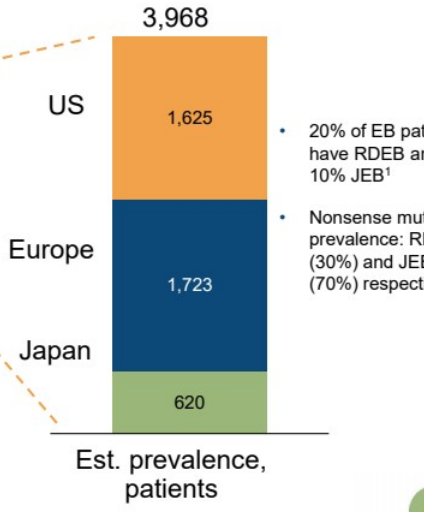
- Mutations in **COL7A1 gene** (RDEB) and **LAMB3** (JEB)
- **Skin tearing/blistering**
- **Impacts other organs including the GI tract (causes malnourishment) and heart**
- **Skin cancer** in RDEB by age 35
- JEB average mortality at 18 months

Disease prevalence

~30,000 total US/EU/Japan RDEB and JEB patients



Geographic breakdown of nonsense mutation patients



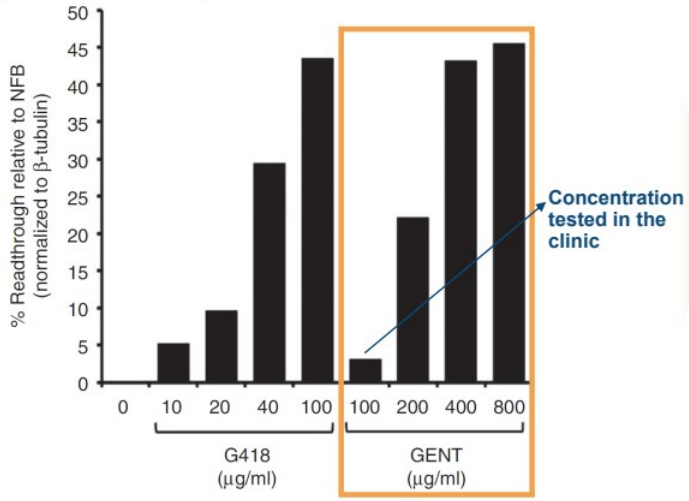
- 20% of EB pat have RDEB ar 10% JEB[1]
- Nonsense mut prevalence: R (30%) and JE (70%) respect

[1] International database of DEB patients with COL7A1 mutations: https://deb-central.org/
[2] Varik.et.al. 2006. *J. Med. Genet* 43: 641

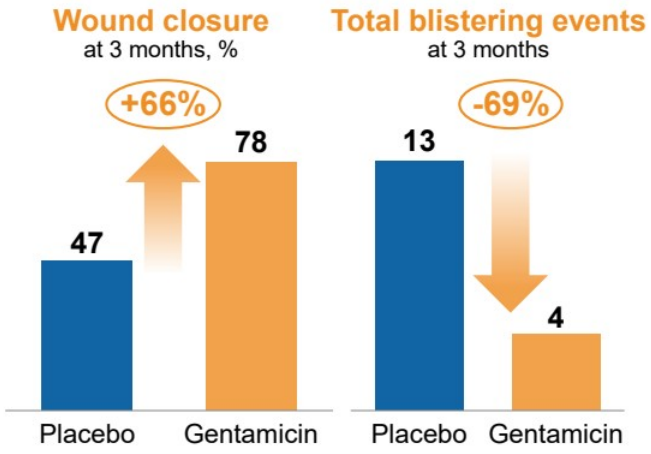
Gentamicin restored COL VII in RDEB patient cells and showed clinical benefit

COL VII protein restoration with gentamicin

COL VII protein expression in RDEB patient fibroblasts[1]



Gentamicin treatment of RDEB patients; n=5; treatment duration: 2 weeks[2]



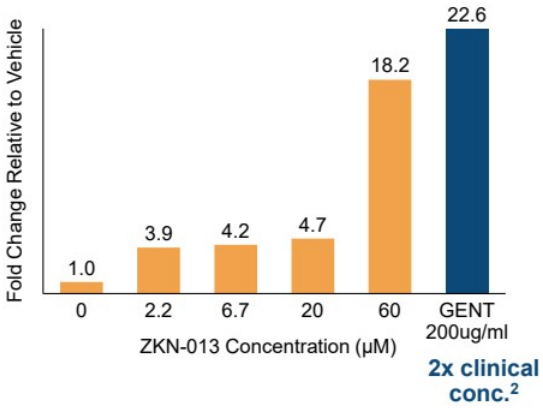
COL VII expression was 20-165% of normal skin

[1] Cogan et al., *Molecular Therapy* (2014)
[2] Woodley, DT. *J Clin Investig* 2017, 127, 3028-3038
RDEB: Recessive Dystrophic Epidermolysis Bullosa

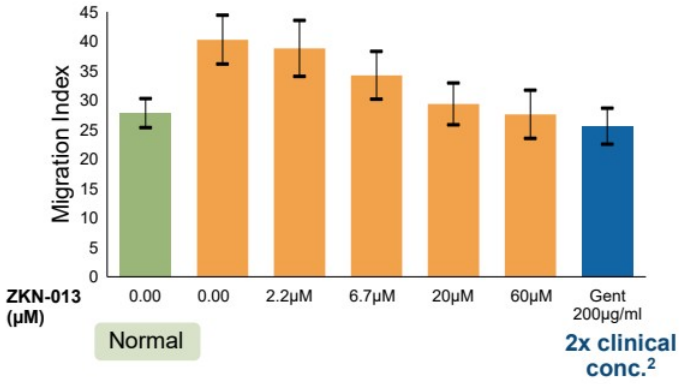
ZKN-013 showed a dose-dependent functional COL VII protein restoration in RDEB patient fibroblasts

ZKN-013 treatment of primary patient fibroblasts[1]

COL VII protein expression in R578X/R578X RDEB fibroblasts with ZKN-013[2]



R578X/R578X patient fibroblast motility after ZKN-013 treatment[3]



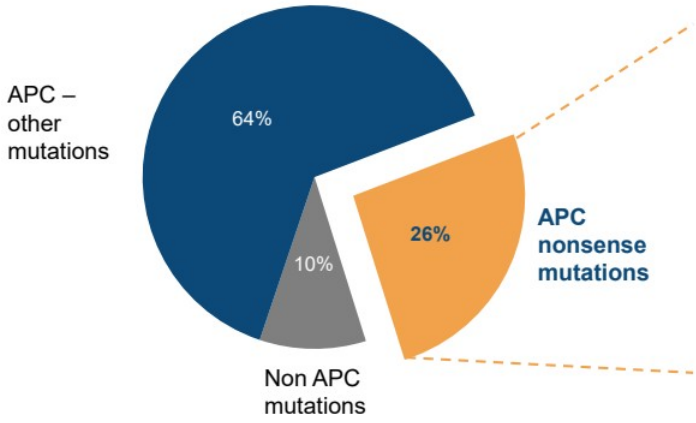
[1]Fibroblasts derived from patients in Woodley et al. J Clin Invest. 2017.
[2]48 hours treatment with media and compounds replaced and refreshed at 24 hours
[3]Fibroblasts cultures suspended and allowed to migrate for 16-20h. Migration index=% of each non overlapping field consumed by cell migration tracks. Data generated in collaboration with Chen lab at USC.
RDEB: Recessive Dystrophic Epidermolysis Bullosa

FAP is a rare GI disease with patients progressing to colon cancer caused by mutations in the APC gene

FAP nonsense mutation market opportunity

FAP patients in the US and Europe by mutation type[1,2]

62,000 – 75,000 Total Patients



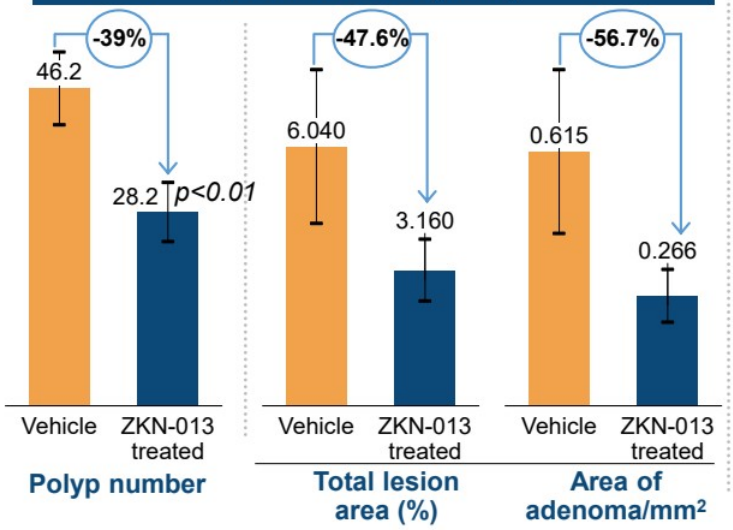
- **No functional APC** (most common mutation is R1450x)
- **Characterized by multiple colon polyps (frequently >1000)**
- Prophylactic colectomy is main treatment
- **Median age of colon cancer** ~40 years, if untreated; secondary GI cancers common

[1] Orphanet Journal of Rare Diseases 2009, 4:22 doi:10.1186/1750-1172-4-22
[2] https://doi.org/10.1016/j.critrevonc.2006.07.004
FAP: Familial adenomatous polyposis; **APC:** Adenomatous polyposis coli

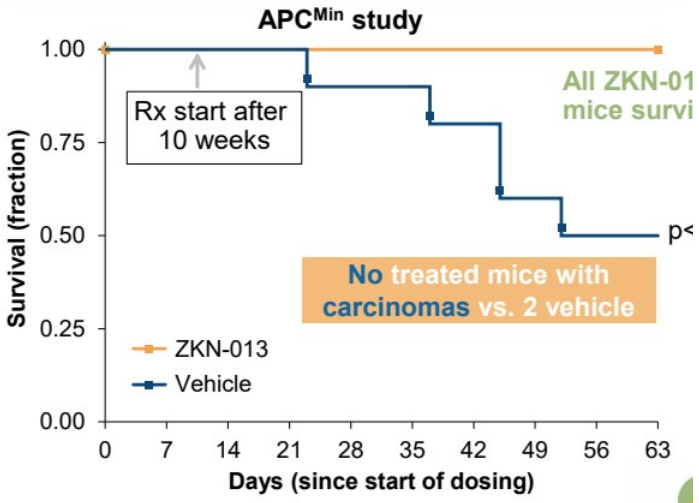
Polyp reduction and survival benefit in ZKN-013 treated APC^{Min} mice suggests robust response in FAP patients

Results for 8 weeks of treatment of APC^{min} mice (FAP model) with ZKN013[1]

Intestinal polyp number and polyp burden post treatment (n=10)[1]



Change in survival post treatment (n=10)[1]



[1]Study conducted at CRO

FAP: Familial adenomatous polyposis; **APC:** Adenomatous polyposis coli

ZKN-013 ready for Phase 1 and expected to achieve sufficient exposure to support efficacy

Exposure at no adverse effect level (NOAEL) of ZKN-013 in rat

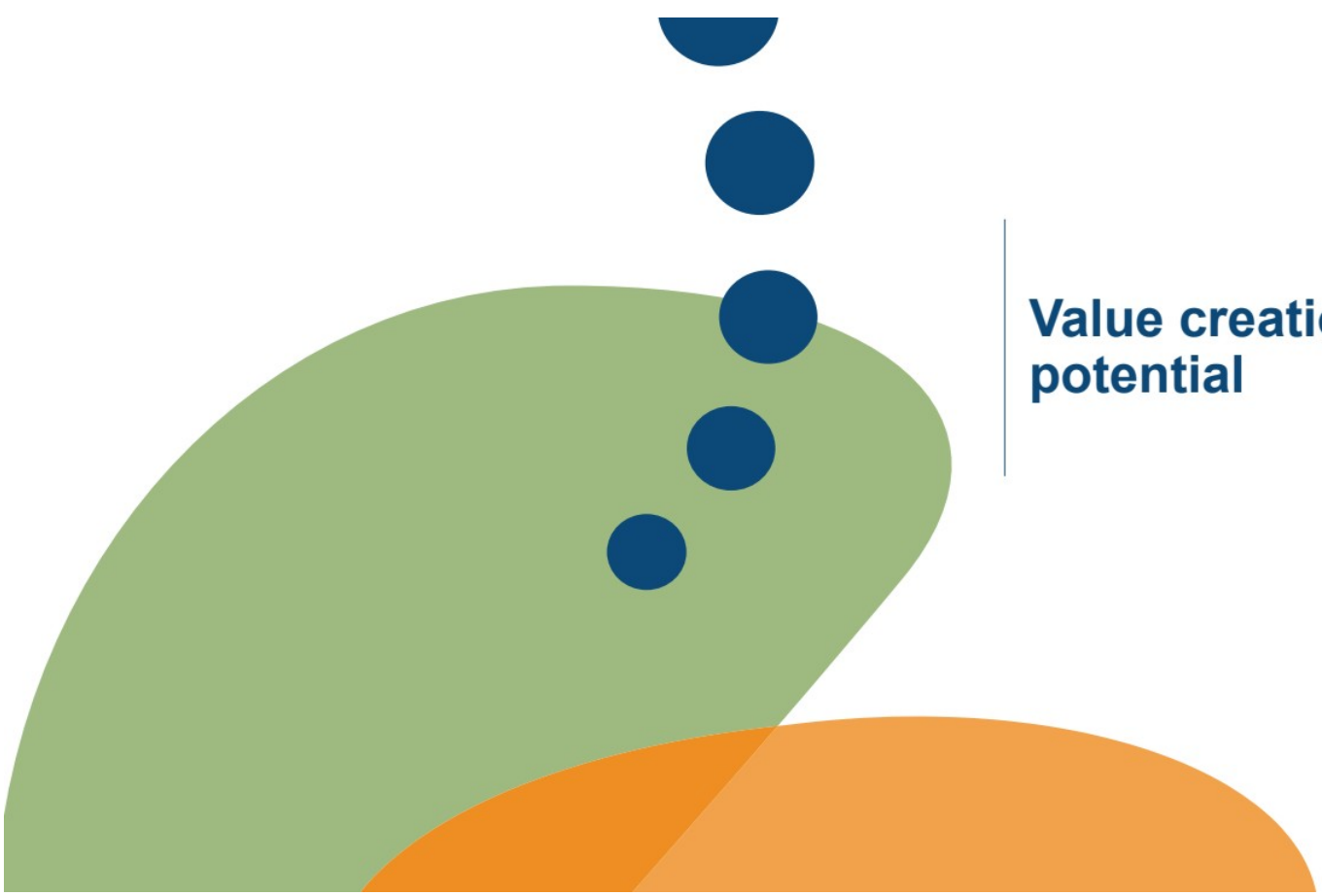
Skin exposure at NOAEL in 14-day non-GLP rat oral DRF study

	Male 30 mg/kg
14-day terminal skin exposure	**19.4 µM**

Summary of preclinical safety findings

- Rats and dogs chosen as tox species based on comparable protein binding, *in vitro* metabolism and drug stability in hepatocytes
- NOAEL in male rats is 30 mg/kg in 28-day GLP tox study
- **Findings consistent with toxicity profile of azithromycin**
- ZKN-013 clean in all genotoxicity studies

FDA approved Phase 1 start in April 2023

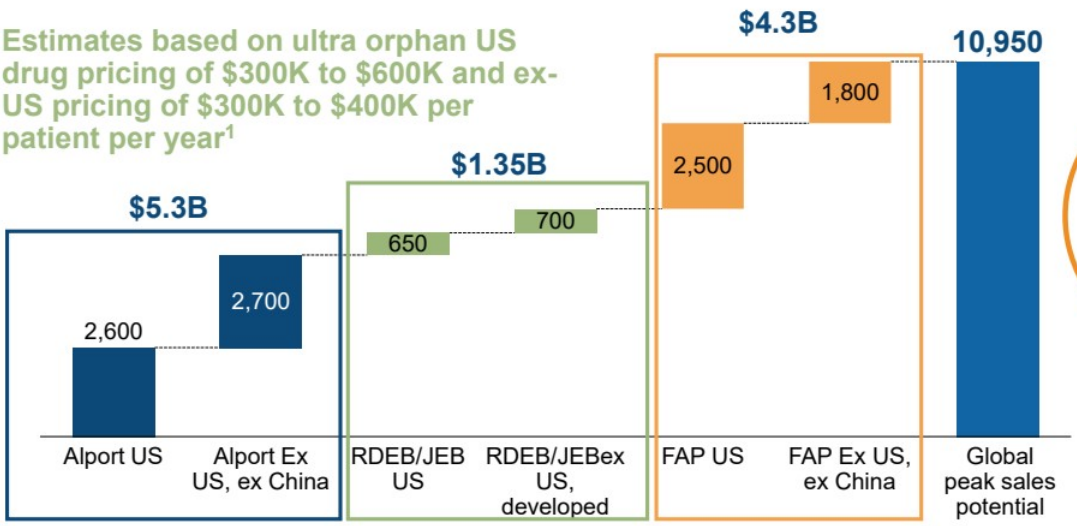


Value creation potential

Substantial potential of three clinical stage programs leading with Alport syndrome

Estimated peak sales potential of current rare disease clinical programs, $M

Estimates based on ultra orphan US drug pricing of $300K to $600K and ex-US pricing of $300K to $400K per patient per year[1]



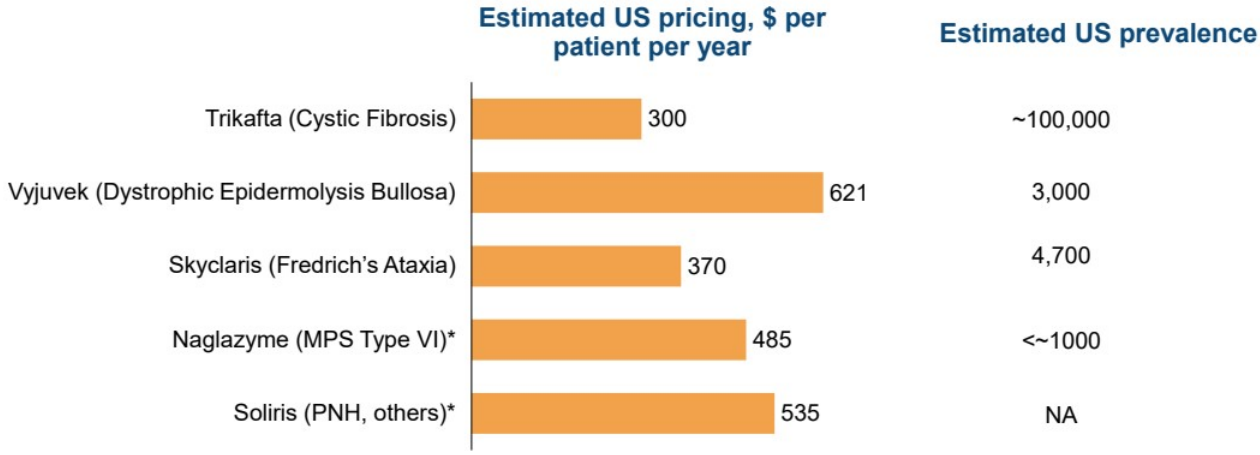
Total US : $5.75B

Alport US: $2.6B

[1]Recent orphan US drug pricing range from $300K to $570K for orphan drugs and >$800K for gene therapy drugs

Strong rare disease drug pricing supports estimated sales potential

Examples of US rare disease drug pricing



Multiple upcoming milestones in remainder of 2023

	1H 2023	2H 2023
Alport Syndrome (SC ELX-02)	✓Enrollment start ✓Initial results from Phase 2 trial	• IND Submission • End of Phase 2 FDA meeting • Full results from Phase 2 • Initiate pivotal trial
RDEB/JEB (ZKN-013)	✓IND submission	• Phase 1 start
FAP (ZKN-013)		

Cash expected to be sufficient to fund operations into 4Q23

RDEB/JEB: Recessive Dystrophic/Junctional Epidermolysis Bullosa; **FAP**: Familial adenomatous polyposis

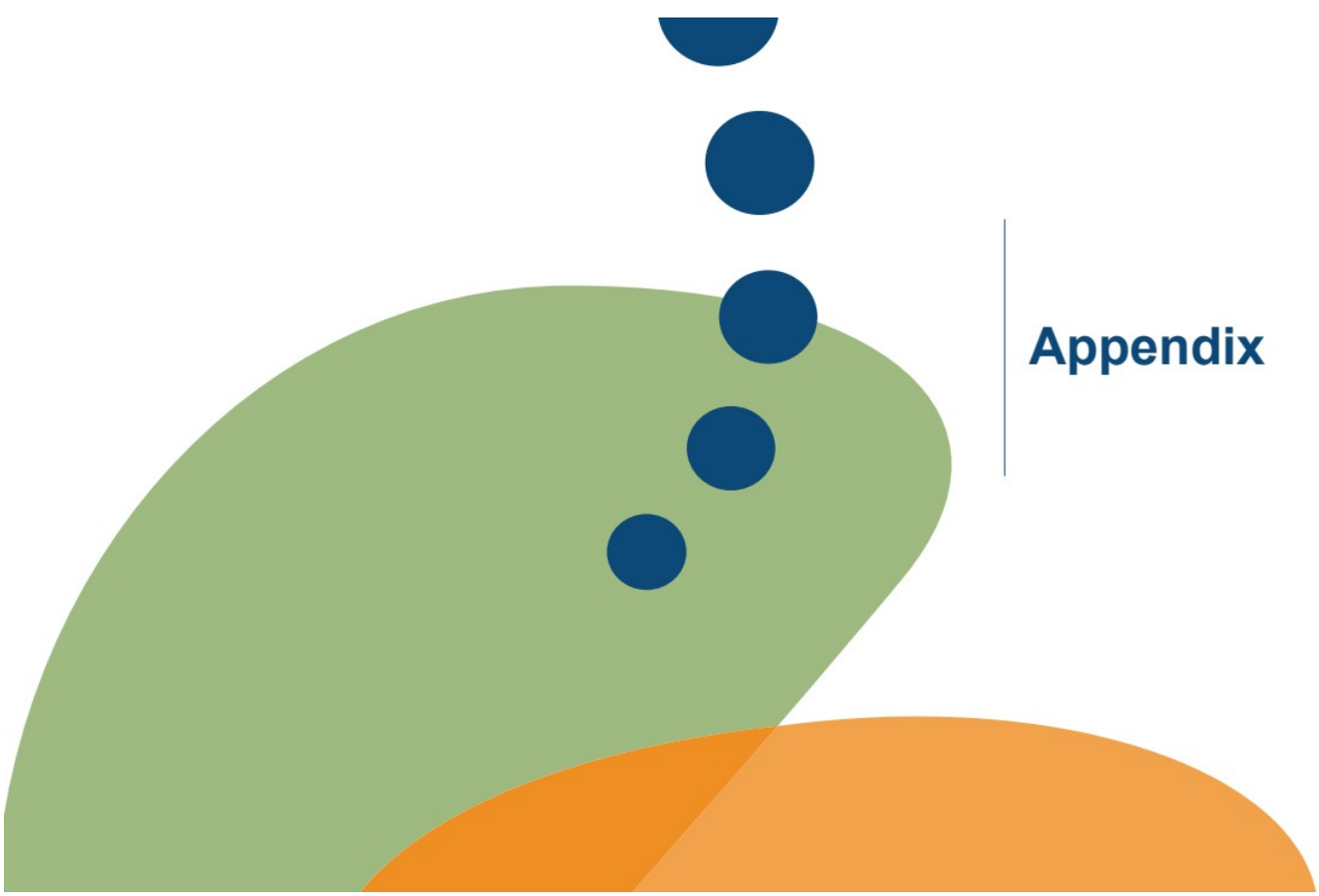
Clinical stage small molecule gene therapy biopharma poised for value creation

Small molecule **genetic therapies** for nonsense mutations proven to restore full-length proteins

ELX-02: Ready for **Alport Syndrome pivotal study** with **biopsy confirmed disease regression.** Preclinical POC in **ADPKD***

ZKN-013: Oral agent ready for **Phase 1** start; robust preclinical efficacy in **RDEB** and **FAP. Potential in ADPKD****

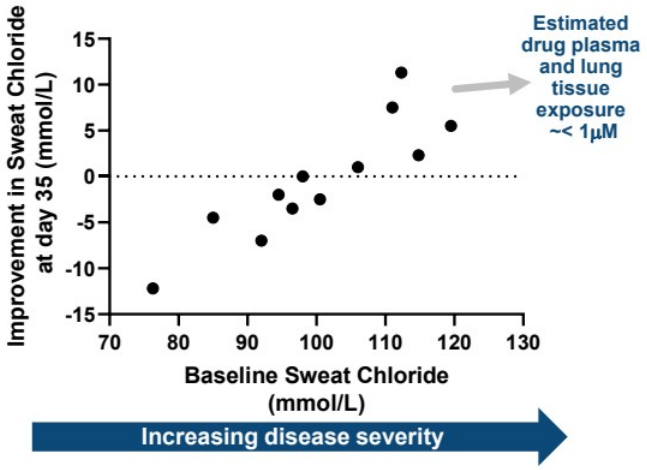

Eloxx
PHARMACEUTICALS


Appendix

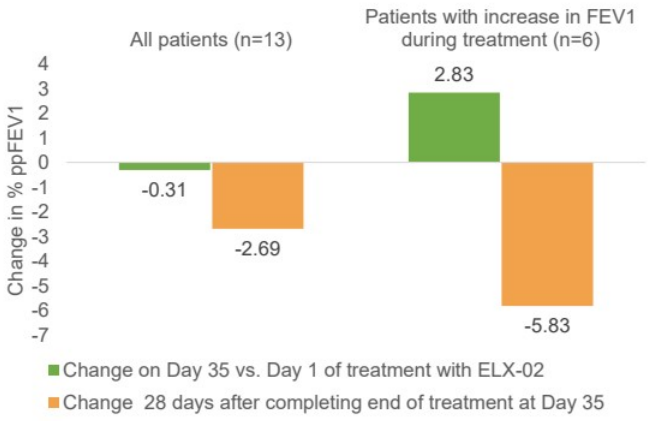
ELX-02 efficacy and biologically activity in CF patients stronger than predicted

Results from Phase 2 trial in CF patients with ELX-02 1.5mg/kg daily and Ivacaftor

Biological activity: Change in sweat chloride vs. baseline sweat chloride

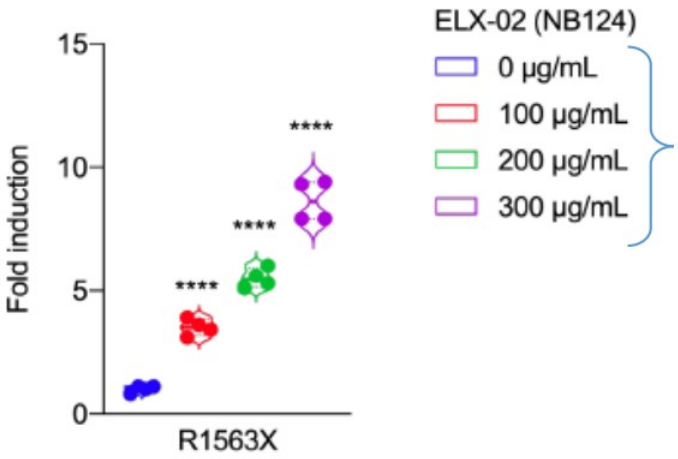


Clinical efficacy: Change in ppFEV1 (%) at end of treatment and safety follow up



High levels COL IV protein restoration observed *in vitro* with ELX-02 after 24 hours

ELX-02 readthrough COL4A5 nonsense mutation in HEK293 cells at 24 hours[1]



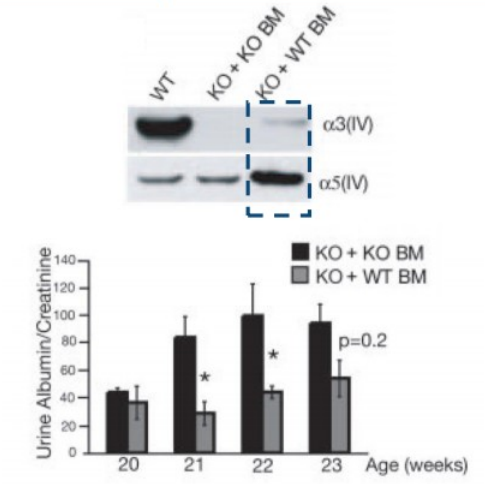
- **>3-fold readthrough in 31 of 32 of COL4A5** mutations tested with ELX-02 and derivatives[2]
- Equivalent to **6% to 15% full length** COL IV protein[1]
- **2- to 4-fold increase in expression** at 48- vs. 24-hr exposure

[1] doi: https://doi.org/10.1101/2021.06.11.448099: Experiment conducted at Washington University by Dr. Jeff Miner
[2] additional mutations tested in same system and lab at Washington university

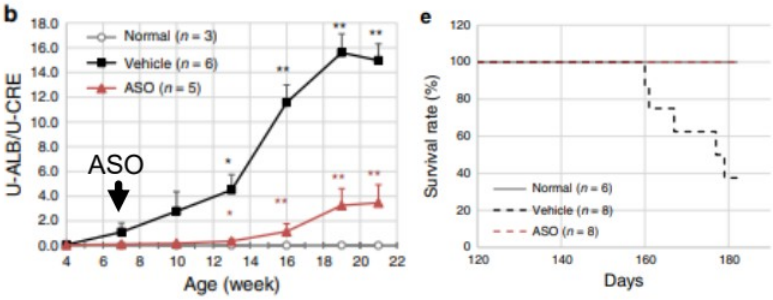
Minimal COL IV restoration sufficient for rapid and large proteinuria reduction in Alport mouse models

Treatment effect of COL IV protein restoration in Alport mouse studies

COL IV A3 bone marrow treatment of C57BL/6 Alport mice over 3 weeks[1]



Single dose exon skipping therapy in nonsense mutation Alport mouse[2]



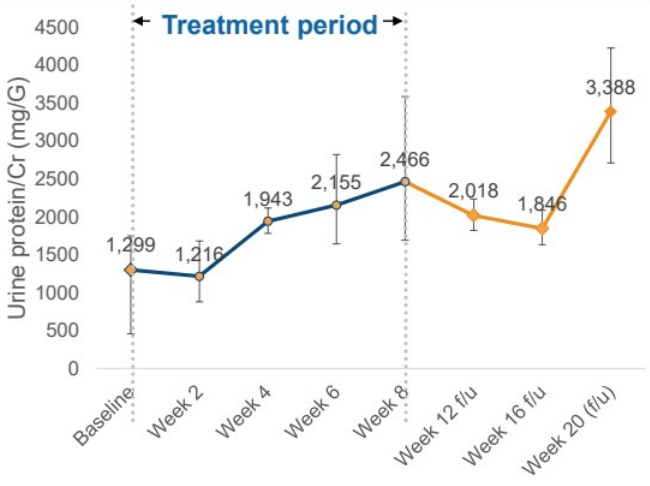
[1] JASN November 2009, 20 (11) 2359-2370. Wild type (WT) Bi-weekly COL4A3 +/- bone marrow (BM) treatment in C57BL/6 knockout mice aged 20 weeks over 3 weeks. treated mice: n=4; Knockout untreated mice: n=3 (*p<0.05)

[2] *Nat. Commun.* 11, 2777. Yamamura et. Al 2020https://doi.org/10.1038/s41467-020-16605-x. (* p<0.05; **p<0.01)

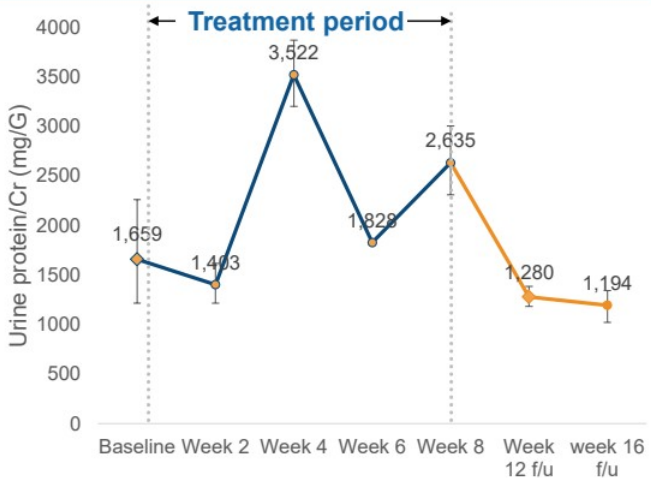
No change in other 2 patients after ELX-02 treatment

Proteinuria change in patient 4401-01 and 4402-01

Patient 4401-01 UPCR change over treatment



Patient 4402-01 UPCR change over treatment



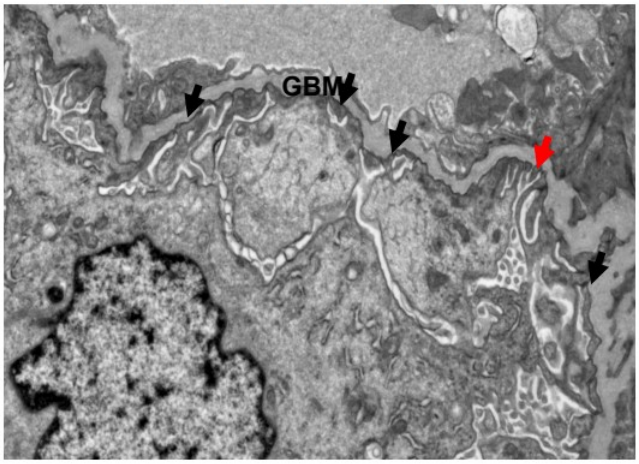
Responder biopsies shows disease regression with improvement in podocyte foot process effacement

TEM sample images from kidney biopsies of patient 4401-02

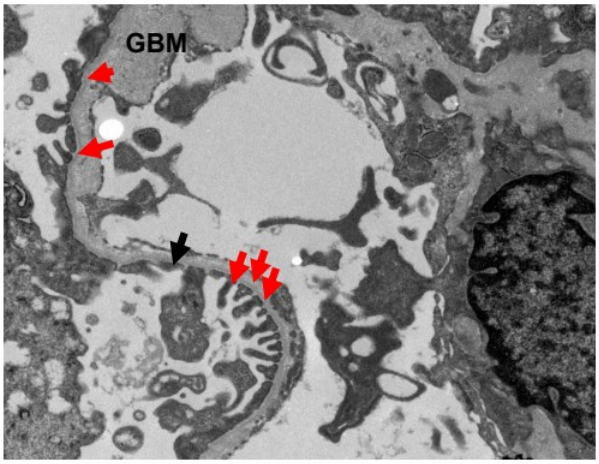
= foot process

= effaced foot pr

Pre-treatment: Widespread podocyte foot process effacement



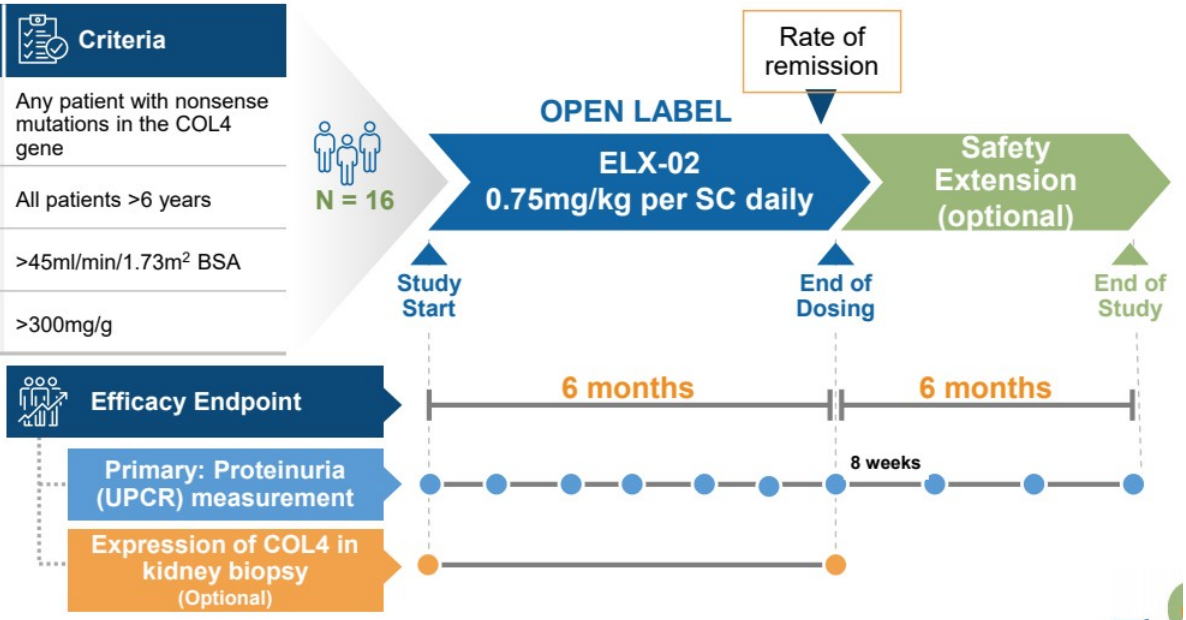
Post-treatment (Day 60): Segmental podocyte foot process effacement



TEM images and analysis done at Mayo Clinic by kidney pathologist on a blinded basis

Disease regression in all patients and 33% proteinuria remission rate in Phase 2 supports advancing to pivotal study

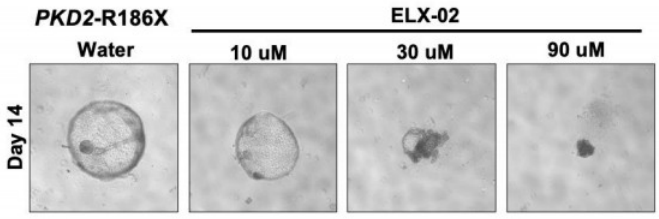
Inclusion Parameters	Criteria
Genotype	Any patient with nonsense mutations in the COL4 gene
Age	All patients >6 years
eGFR	>45ml/min/1.73m^2 BSA
Proteinuria	>300mg/g



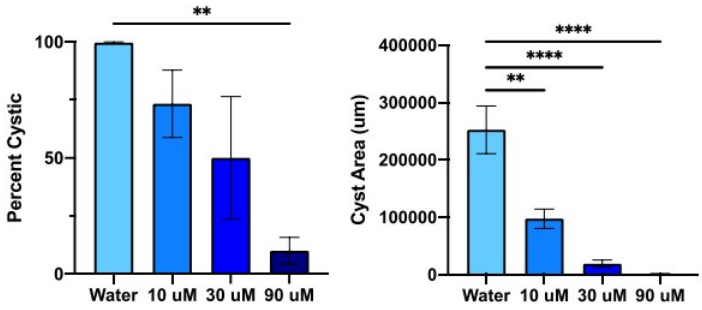
ELX-02 reduced in kidney cyst burden in Polycystic kidney disease organoids in preventative setting

Treatment effect on iPSC model harboring PKD2 nonsense mutation R186X*

iPSC cells treated with ELX-02**



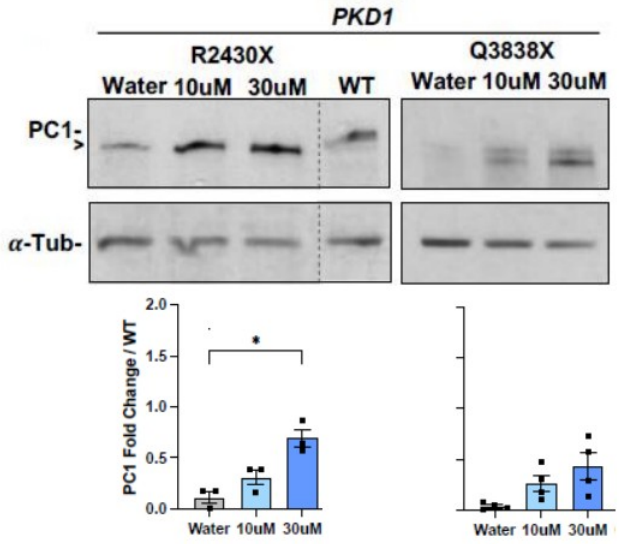
Cyst burden reduction when treated with ELX-02**



*Presented at ASN Kidney Week 2021. ABSTRACT: TH-OR39 November 04, 2021 | Location: Simulive, Virtual Only Abstract Time: 04:30 PM - 06:00 PM
**Single organoids transferred to suspension culture 96-well plates. Treatment is initiated and cyst formation monitored over 14 days.

ELX-02 treatment of ADPKD kidney organoids results in increase PKD1 protein levels

PKD1 mutant organoids treated with ELX-02 for 14 days*

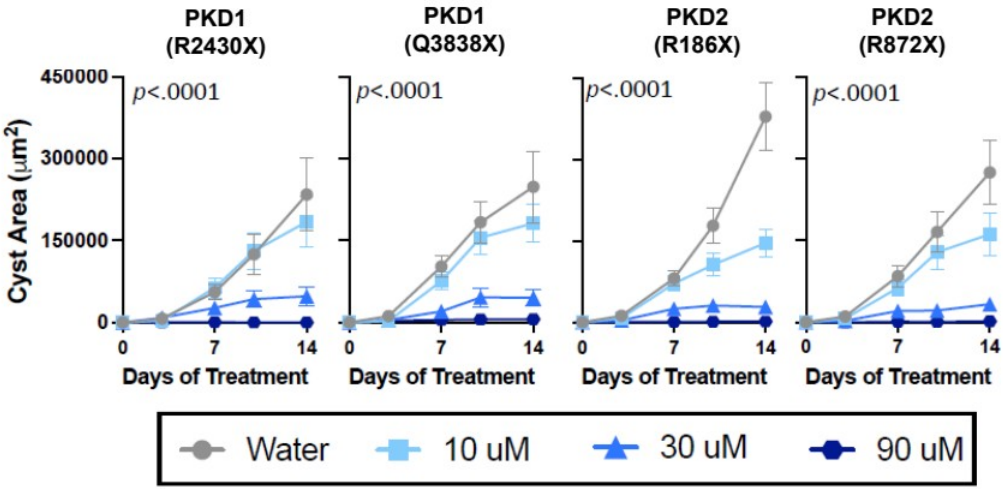


*Data generated in collaboration with Freedman lab at University of Washington.

ELX-02 reduced cyst formation and growth in human iPSc derived kidney organoid models of ADPKD

ELX-02 mediated read-through in nonsense mutant PKD1 and PKD2 organoids*

Prophylactic mode – ELX-02 treatment initiated prior to cysts formation

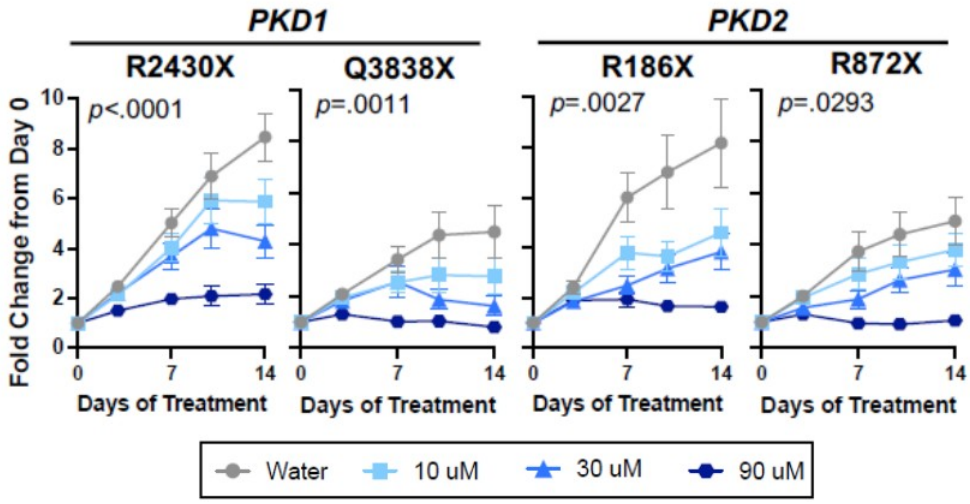


*Data generated in collaboration with Freedman lab at University of Washington. Single organoids transferred to suspension culture 96-well plates. Treatment is initiated and cyst formation monitored over 14 days.

ELX-02 treatment of ADPKD kidney organoids inhibits growth of pre-existing cysts

ELX-02 mediated read-through in nonsense mutant PKD1 and PKD2 organoids*

Therapeutic mode – ELX-02 treatment initiated after 7 days of cysts formation



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