Small Molecule Genetic Therapies for Rare Diseases

Corporate Presentation

April 2024

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.

Eloxx PHARMACEUTICALS

Value drivers are two clinical stage disease-modifying small molecule therapies supported by global partnership

Proprietary small molecule therapies proven to restore full-length proteins in rare nonsense mutation driven genetic disease

ELX-02: Phase 3 ready with confirmation of disease regression in POC study in Alport syndrome patients

- Validated MOA; Disease modifying
- Orphan Drug Designation
- No approved therapy
- >20,000 patients

ZKN-013: Open IND for oral agent ready for **Phase 1** start; robust preclinical efficacy in **RDEB** and **FAP**

- Exclusively licensed to Almirall
- Validated MOA; Disease modifying
- In vivo survival benefit

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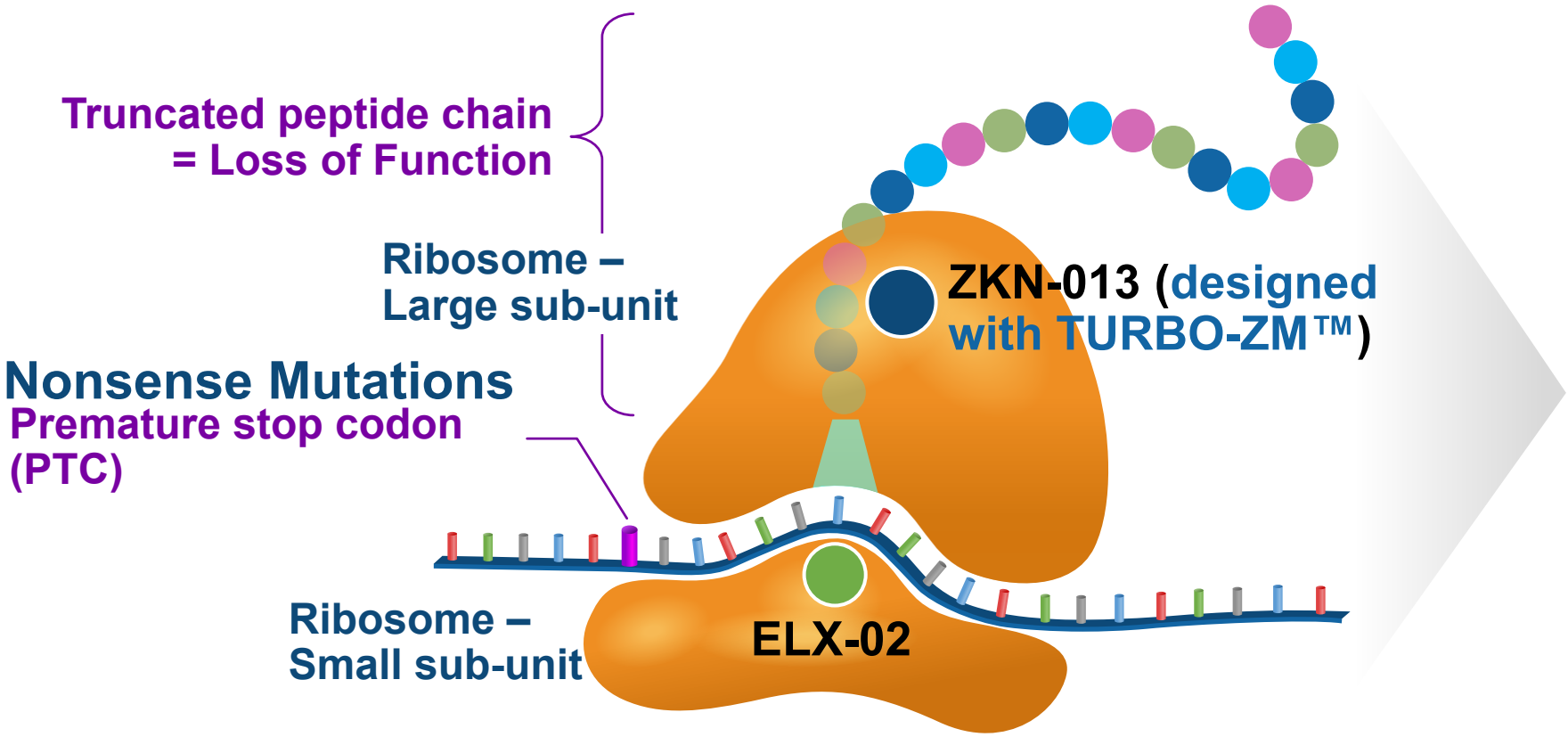
First in class RNA-targeted therapeutics that induce full-length functional proteins

MOA: Restore full-length protein by inducing readthrough of premature stop codon mutations



ELX-02 and ZKN-013 rationally designed with superior efficacy and safety to gentamicin and erythromycin

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ZKN-013 exclusively licensed to Almirall unlocks significant value from pipeline validating TURBO-ZM platform

- Almirall is dermatology focused mid tier company with >$1B revenues
- Global Development and commercialization Rights to ZKN-013 provides entry into rare diseases with RDEB and FAP
- Eloxx eligible to receive up to $470 million in development, regulatory and sales milestones
- Tiered royalties on sales with peak sales potential of >$5 billion
- Total deal net present value to Eloxx is >$400M

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ELX-02: Novel aminoglycoside with gentamicin mechanism of protein induction by premature stop codon readthrough

Gentamicin has demonstrated proof-of mechanism in >36 genetic diseases

Diseases	Evidence	Readthrough Agent(s) Tested	
		Macrolides	Aminoglycosides
Familial Adenomatous Polyposis (FAP)	Clinical[1]	Ery, Tyl	Gen
Cystic Fibrosis Class 1	Clinical[2]	Tyl	Gen, G418
Duchenne Muscular Dystrophy	Clinical[3]		Gen
Dystrophic Epidermolysis Bullosa (RDEB)	Clinical[4]		Gen, G418
Lysosomal Storage Disorders, e.g., MPSI (Hurler), cystinosis	*ex vivo*[5]		Gen, G418
Rett Syndrome	*ex vivo*[5]	Ery	Gen
Spinal Muscular Atrophy (SMA)	*ex vivo*[5]	Azm, Ery	Gen
Ataxia-Telangiectasia (ATM)	*ex vivo*[5]	Ery	Gen
Usher syndrome/retinitis pigmentosa (RP)	*in vivo* Preclinical[6]		Gen, G418

Macrolides: Erythromycin (Ery); Tylosin (Tyl); Azithromycin (Azm)
Aminoglycosides: Gentamicin (Gen); Geneticin (G418)

[1]Kariv, R. Ann. Oncol. 2018, 29, suppl3; [2]Sermet-Gaudelus, I. BMC Med. 2007, 5, 5; [3]Malik, V. Ther. Adv. Neurol. Disord. 2010, 3, 379; [4]Woodley, D. J Clin Invest. 2017;127(8):3028, [5]Caspi, M., J Mol Med (Berl). 2016 Apr;94(4):469-82; [6]Goldmann, T, Hum Gene Ther. 2011 May;22(5):537-47.

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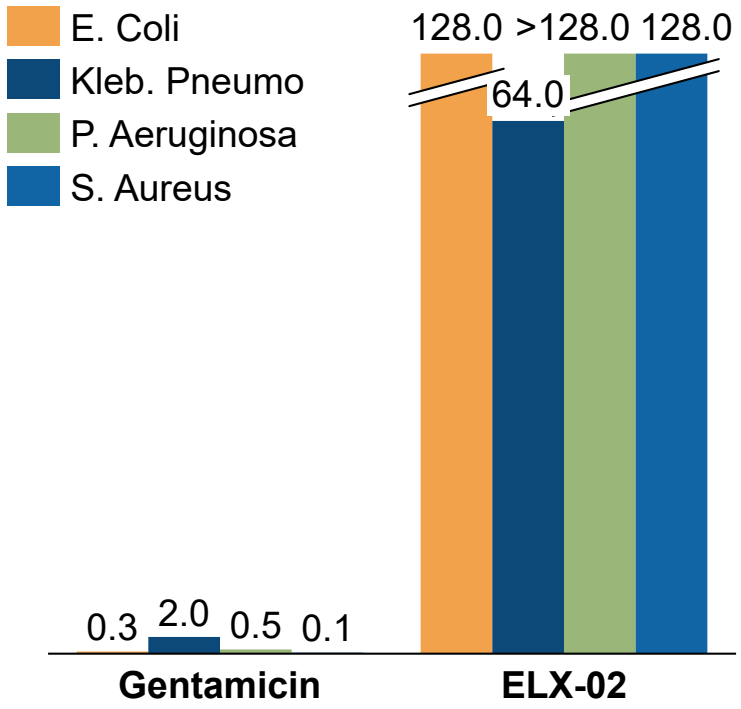
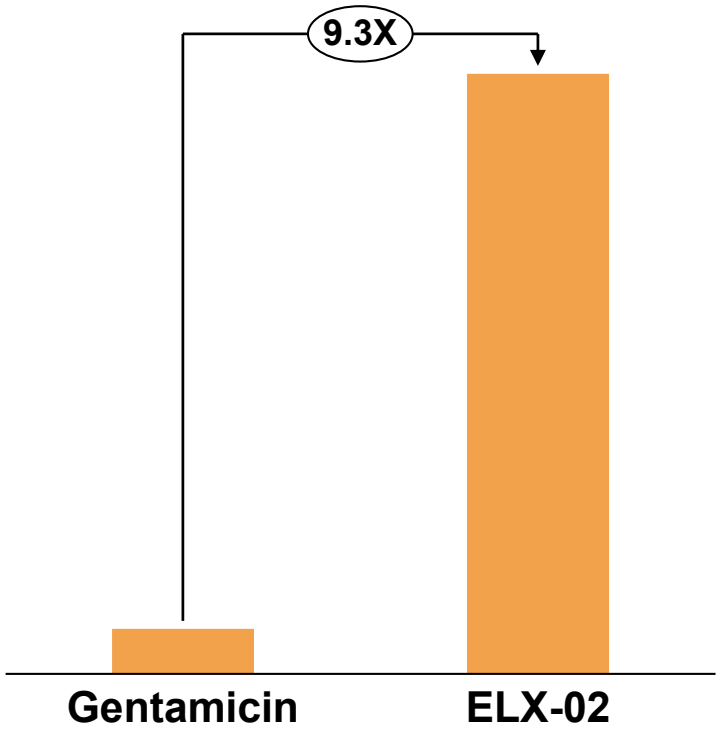
ELX-02 is a novel non-antibiotic readthrough agent designed for superior efficacy and safety

ELX-02's significantly lower anti-mitochondrial activity key for superior safety

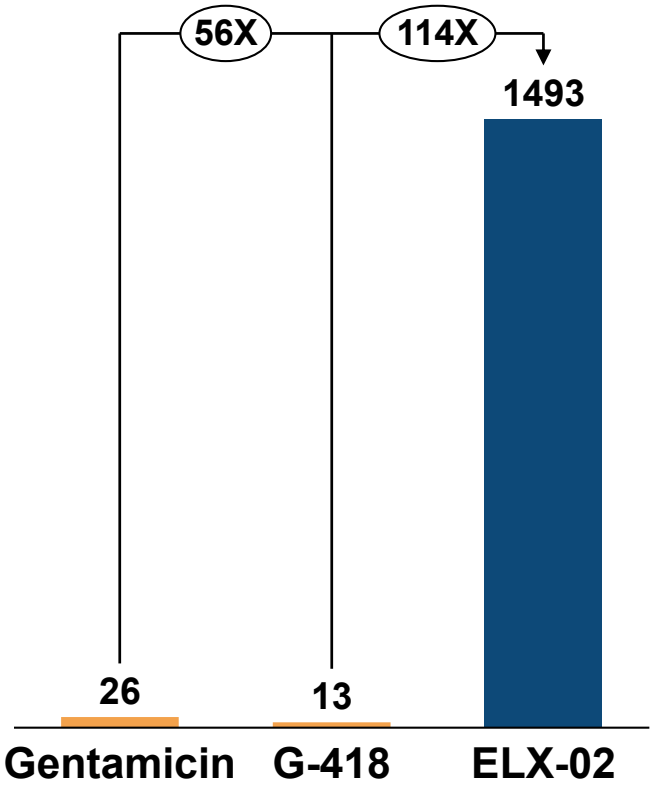
Relative ELX-02 antibiotic activity (MIC μg/mL)



Relative ELX-02 readthrough activity[1]



Relative mitochondrial protein inhibition (IC_{50} μM)[2]



1. Readthrough measured in G542X HE cell Dual Luciferase assay
2. Data adapted from: J Med Chem. 2012 Dec 13;55(23):10630-43; Shhulman,et al 2014.

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Why we're excited: Significant preclinical *and* clinical validation with path to commercialization

ELX-02 has delivered on its promise of a nonsense mutation readthrough agent

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

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

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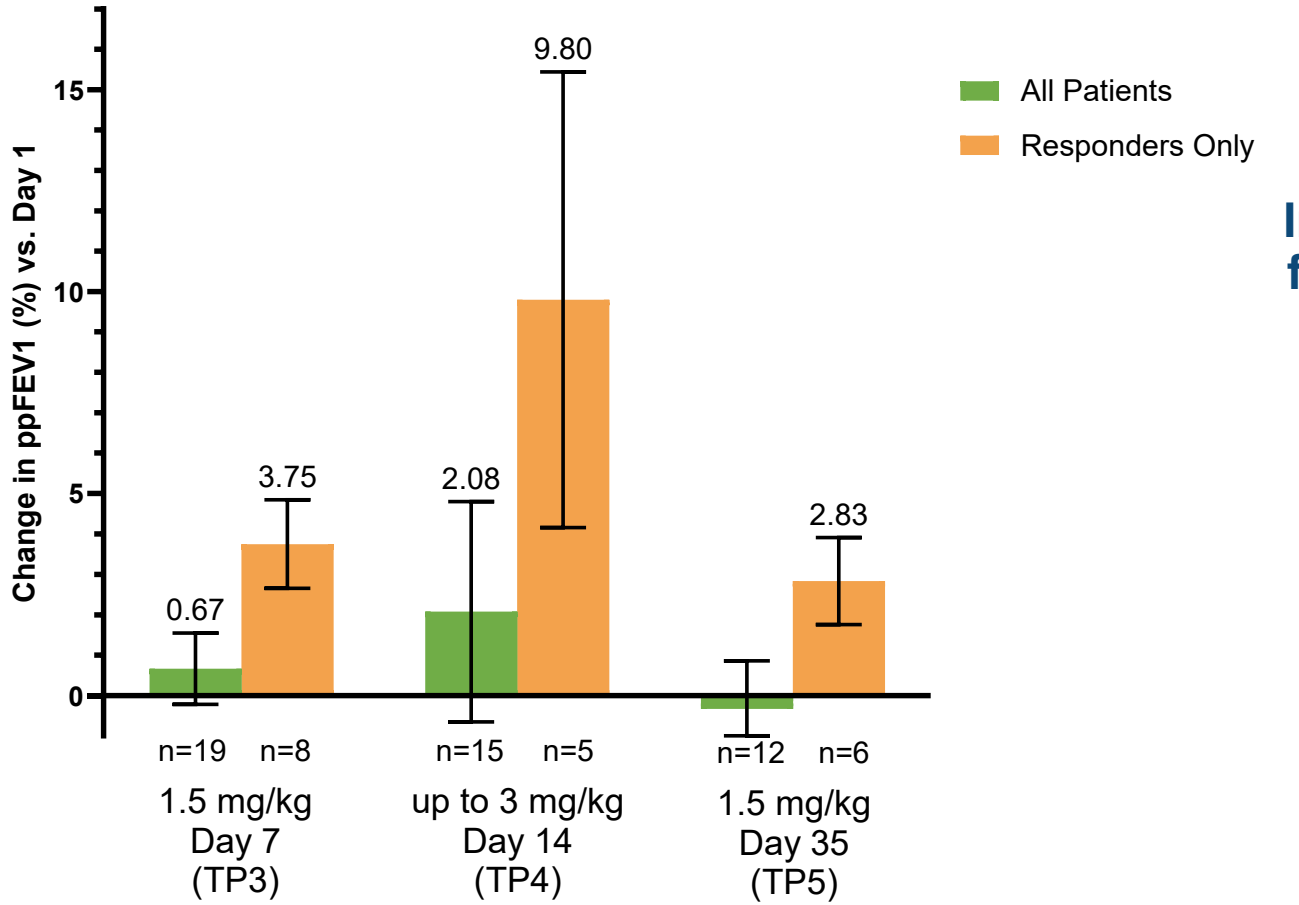
Demonstrated dose dependent proof of clinical activity in nonsense mutation cystic fibrosis (CF) patients

Change in ppFEV1 in nonsense mutation CF patients at end of treatment vs. Day 1 after ELX-02 monotherapy and combination therapy (Phase 2)



Improvement in lung function higher than predicted from preclinical studies

TP3: 1 week treatment with ELX-02 1.5mg/kg/day; TP4: 2 week treatment with ELX-02 dosed up to 3mg/kg/day; TP5: 5 week treatment with ELX-02 dosed 1.5mg/kg/day with ivacaftor

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Strong pediatric and adult safety profile confirmed in 8 clinical trials in 145 subjects (89.4 subject-months exposure)

No nephrotoxicity or hearing loss observed in any patients to date

No ELX-02 related SAEs in Phase 1 and 2 studies at doses up to 7.5 mg/kg in 145 subjects (including 2 pediatric) with no nephrotoxicity or hearing loss

ELX-02 was well tolerated up to 3.0 mg/kg dose across Phase 2 patients (n=40)

- Mild to moderate injection site reactions most common adverse events mostly at higher doses (1.5 mg/kg/day)
- No hearing loss in CF trials at 1.5 mg/kg after 5 weeks mild hearing loss in patients at baseline
- No kidney toxicity in cystinosis patients despite eGFR as low as 44
- No kidney toxicity in Alport patients including 2 pediatric (aged 12 years) patients at 0.75 mg/kg/day

SAE: Serious adverse events

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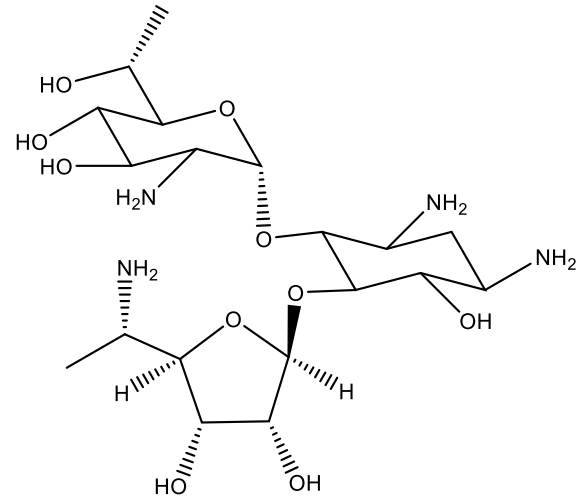
ELX-02: Renal collagenopathies



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ELX-02: Novel genetic therapy to treat Alport patients with nonsense mutations

ELX-02: Novel Eukaryotic Selective Glycoside: Designed for robust Premature Termination Codon (PTC) readthrough

Functional protein restoration proven in pre-clinical and clinical studies

Orphan Drug Designation (also has ODD for CF and Cystinosis)

Treatment resulted in podocyte morphology in 3 Alport patients in UK clinical trial after 8 weeks

Ultra-rare patient population with no approved therapies; Support for UK trial from patients and physicians

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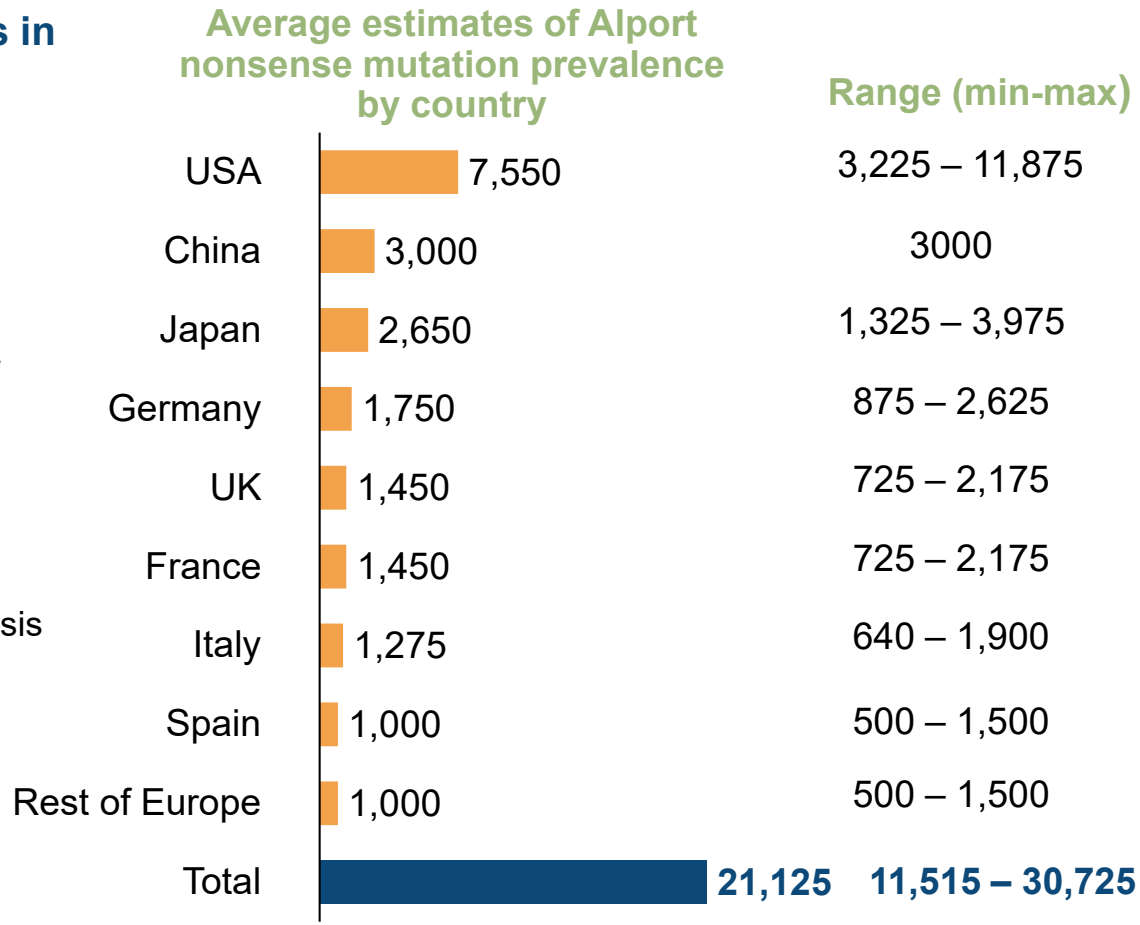
Nonsense mutation Alport Syndrome (NMAS) presents multi-billion opportunity in significant unmet need orphan disease

>20,000 addressable patients with $400-600K/patient/year annual pricing

Nonsense Mutation Alport disease overview[1,2]

- **Rare genetic disease** caused by **nonsense mutations in *COL4A3, COL4A4* and *COL4A5* genes**
  - Truncated Collagen IV trimer in the glomerular basement membrane (GBM) – loss of function
  - Majority of patients have X-linked disease
  - Progressive podocyte loss and kidney failure and hearing loss
- **Collagen IV trimer has ~3 month half-life: Low new collagen induction needed for meaningful improvement**
- **Primarily pediatric disease**
  - Median age of diagnosis of 9 to 20 years
  - Median time to kidney failure of 4 to 12 years from diagnosis
- **No approved therapies**
  - **Limited therapeutic options** (RAAS Inhibition)

Global estimated Alport nonsense mutation prevalence[3]

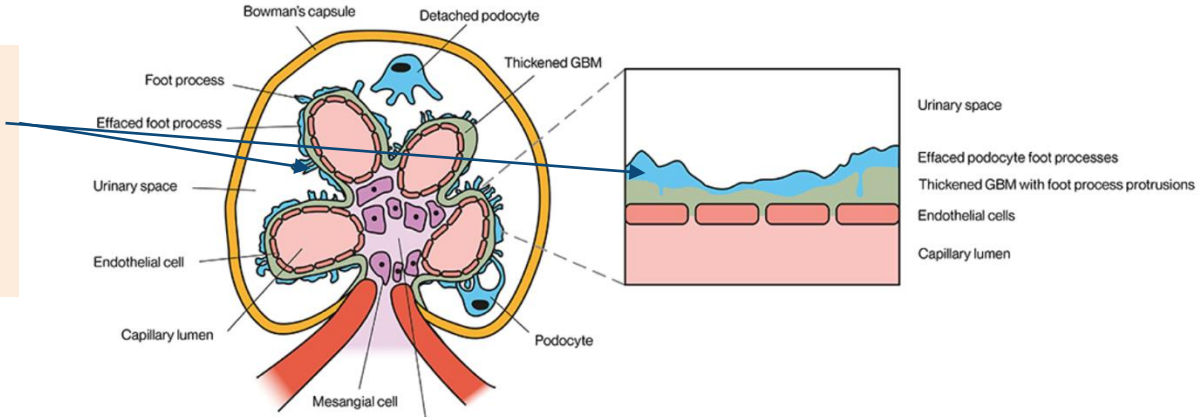


[1]J Am Soc Nephrolv.28(6); 2017 JunPMC5461786
[2]J Clin Invest 1995 Sep;96(3):1404-13
[3]JASN 32(9):p 2273-2290, September 2021.

Progressive podocyte Foot Process Effacement causes proteinuria and is hallmark of NMAS

Collagen IV secretion by podocytes regulates signaling pathways between podocytes and the GBM resulting in formation of foot processes

Podocyte foot process effacement causes proteinuria in Alport syndrome



Definition:

- Thickened, split and irregular GBM
- Enlarged, **flattened foot processes with loss of the slit diaphragms** leading to proteinuria

Cause in Alport:

- Absence of any one of the Col IV a3, a4 or a5 proteins
- Altered GBM morphology and loss of podocyte foot process architecture

Progression:

- *Segmental and Moderate:* Milder diseases (lower UPCR)
- *Widespread:* Severe disease (1.5 - 3.0 g/g UPCR)
- *Global:* Effacement in all glomeruli before podocyte death (>3g/g UPCR)

Alport Research Hub - https://sites.manchester.ac.uk/alport-hub/about-alport-syndrome/

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Large pediatric population given natural history of early diagnosis and rapid progression

Nonsense mutation Alport syndrome patients with truncating mutations are diagnosed early and progressed rapidly to proteinuria and kidney failure

RaDaR National Registry of Rare Kidney Diseases

Nonsense mutation Alport Syndrome Type	Median Age at diagnosis (years)	Mean eGFR at diagnosis (ml/min/1.73m2/year)	Median annual eGFR decline (ml/min/1.73m2/year)	Median UPCR, g/g before eGFR>30	Mean age at ESRD (years)
X-linked COL4A5 Males	19.6 years (IQR: 8.7 to 29.6)	61.4±61.1	-6.9 (IQR: -8.7 to -4.2)	1.4 (IQR:0.9 -3.0)	31.9±10.9
Autosomal Recessive COL4A3/4 Males	7.0 years (IQR: 4.6 to 22.9)	nm	-22.4 (IQR: -29.9 to -14.8)	1.9 (IQR:0.9 -3.1)	20.1±3.2
Autosomal Recessive COL4A3/4 Females	4.7 years (IQR: 2.7 to 15.2)	nm	-7.1 (IQR: -10.7 to -3.4)	1.9 (IQR:0.9 -3.1)	23.8±10.9

7x to 22x worse than in healthy subjects; 4x to 7x worse than in IgaN patients

20 to 40 years earlier than missense Alport patients

IQR= Interquartile range
Source: UK Registry of Rare Kidney Diseases (RaDaR)

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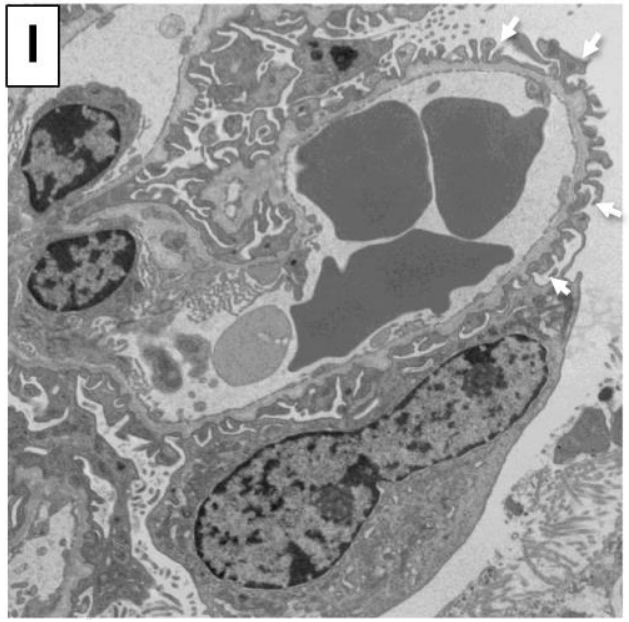
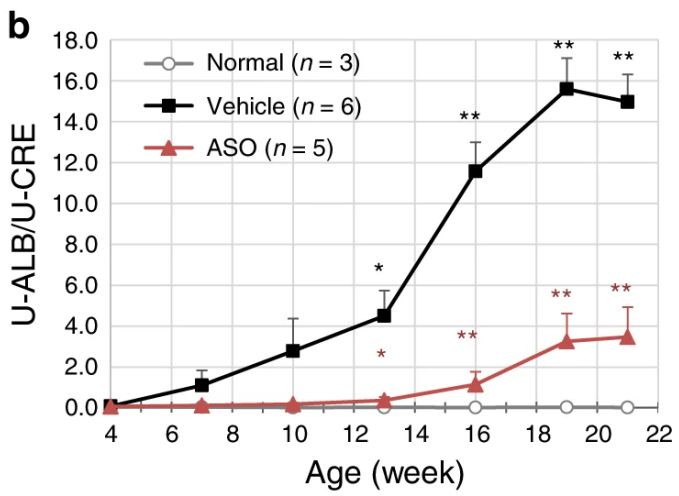
Collagen induction in Col4a5 knockout mice reduced foot process effacement with improved albuminuria and survival

Exon skipping treatment in Col4a5 exon 21 fs mutation mouse mouse model*

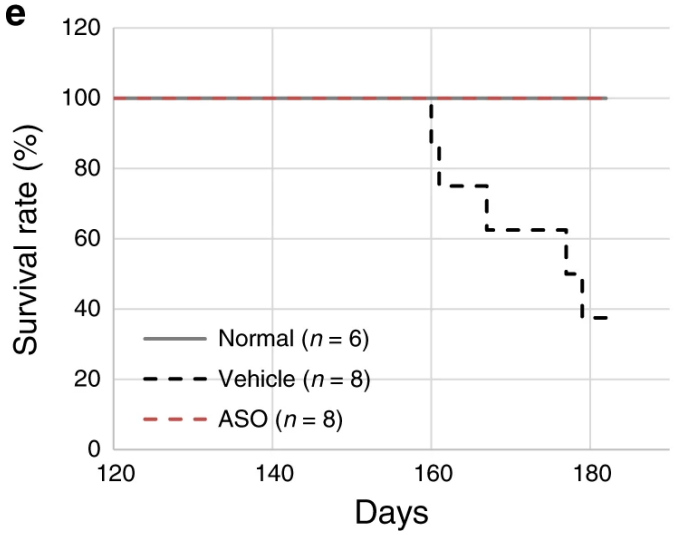
Impact on Podocyte foot process effacement



Albumin/Creatinine ratio



Survival



Col4a5 nonsense mutation mouse model treated from 4 weeks age to 20 weeks (16 weeks treatment duration) had improved podocyte foot process effacement, albuminuria, and survival

* Col4a5 mutant mouse model with c.1411C > T (p.Arg471*) in exon 21 and this mutation is equivalent to the nonsense mutation of c.1411C > T (p.Gln471*) of human COL4A5

- p<0.05; **p<0.01

[1] *Nat. Commun.* 11, 2777. Yamamura et. Al 2020https://doi.org/10.1038/s41467-020-16605-x.

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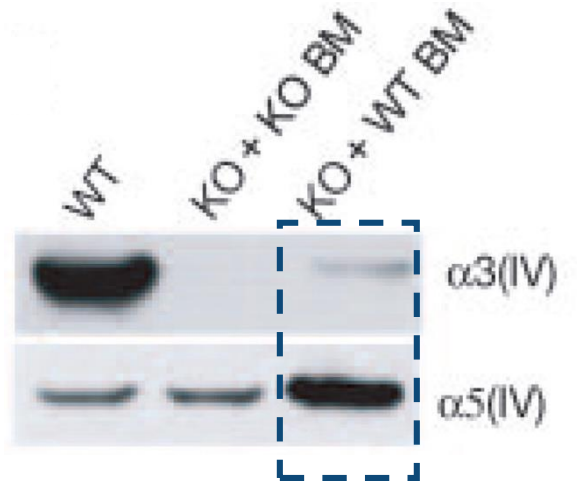
Col4a3 restoration in mice also reduced foot process effacement and lowered albuminuria

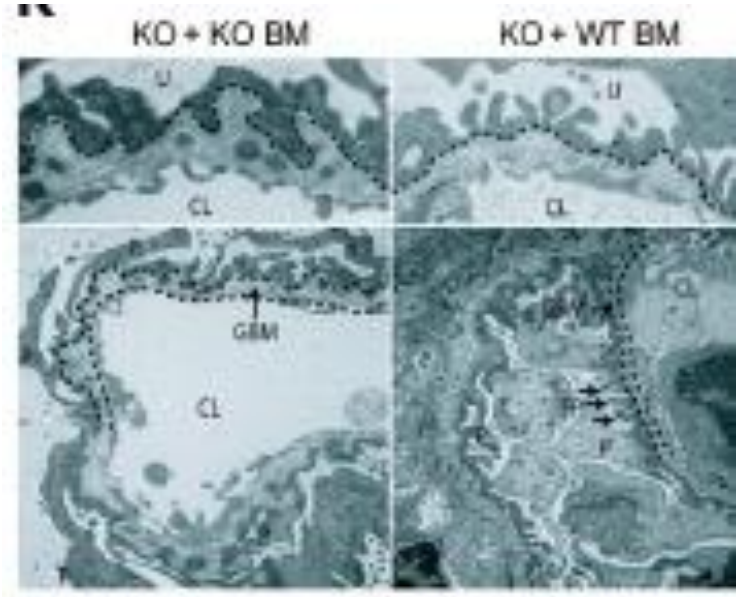
Bi-weekly Col4a3$^{+/-}$ bone marrow (BM) therapy in C57BL/6 Col4a3$^{-/-}$ knockout mice at age 20 weeks for 3 weeks[1]

Western blot of COL4A3[2]

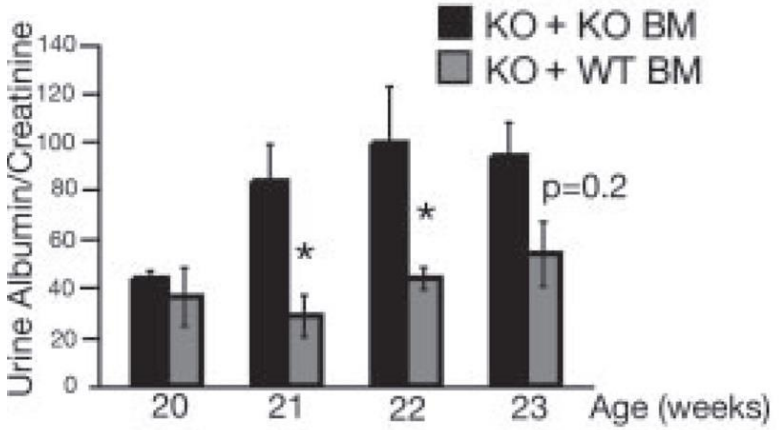


Treatment effect[2]

Change in Podocyte foot process effacement



Change in AUCR



[1].JASN November 2009, 20 (11) 2359-2370.
2 Wild type (WT) COl4A3 treated mice: n=4; Knockout treated mice: n=3
*p<0.05

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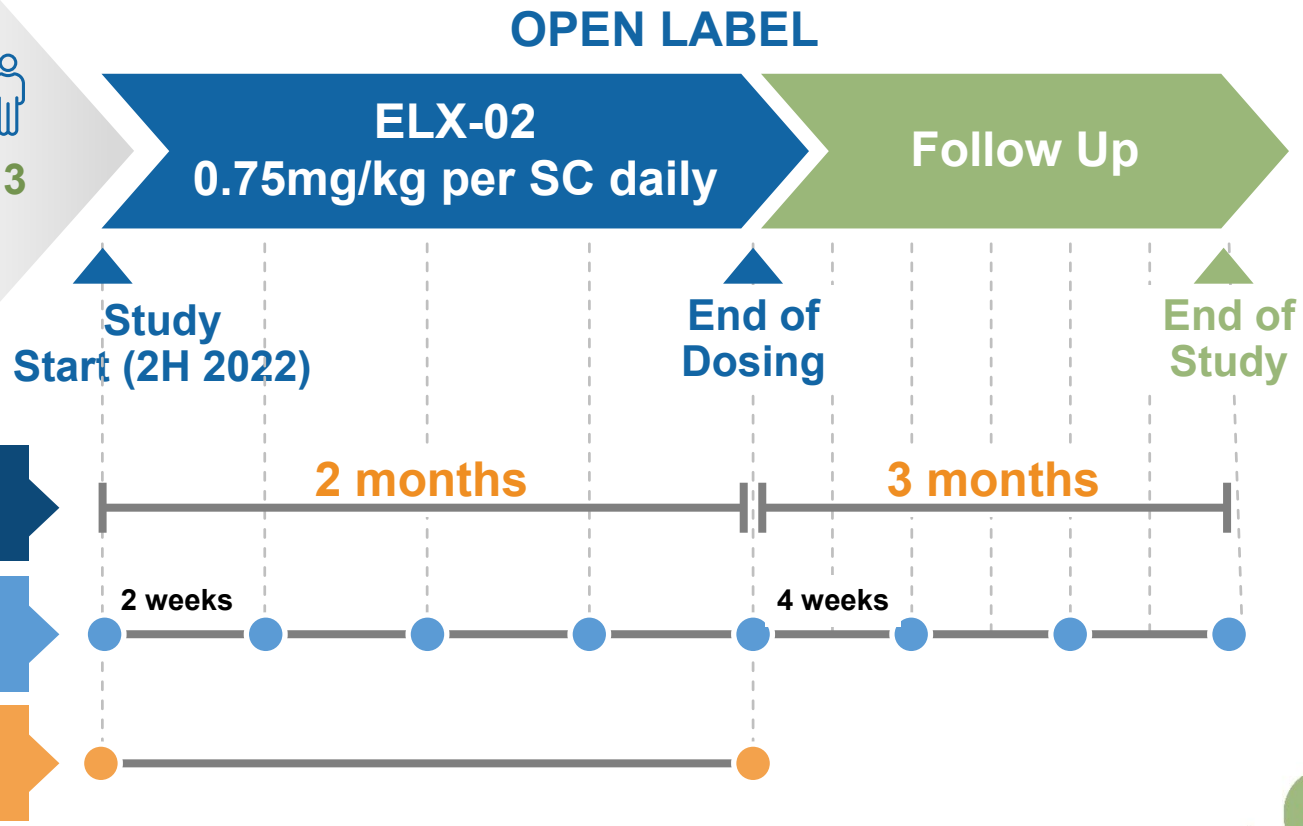
Completed Proof of Concept Phase 2 UK study of ELX-02 in Patients with Alport Syndrome

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

n= 3



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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)	UPCR (mg/g)	Col4A5 staining in the GBM*
4401-01	12	M	COL4A4	**p.Ser969X / p.Ile29_Leu30del**	Enalapril 2.5 mg QD	0.7	1299	Global loss
4401-02	12	M	COL4A4	**p.Ser969X / p.Ile29_Leu30del**	Enalapril 32.5 mg QD	0.5	1646	Global loss
4402-01	18	F	COL4A4	**p.Ser969X / p.Arg1682Trp**	Enalapril 5 mg QD	1.31	1645	Partial Loss

RaDaR National Registry of Rare Kidney Diseases

UKKA UK Kidney Association

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

*All Patients were compound heterozygous with loss of function on both alleles. No Col4A5 protein staining observed in GBM prior to treatment indication loss of function on both alleles. 4402-01 assessment by second Mayo clinic pathologist

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Treatment for 8 weeks demonstrated reduction in foot process effacement and proteinuria

ELX-02 is first drug to show a disease regression in Alport patients

Increase in COL4A5 protein expression in the glomerular basement membrane (GBM) in **all patients**

Qualitative and quantitative improvement in kidney morphology in all patients; 60% average improvement in podocyte foot process effacement improvement

UPCR improvement in 2/3 patients and UPCR stabilization in third patient: 37.6% reduction at end of treatment (48% average reduction) in1 patient. 25% reduction at 4- and 8-weeks after end of treatment in 2nd patient

Overwhelming KOL support for advancing to pivotal trial

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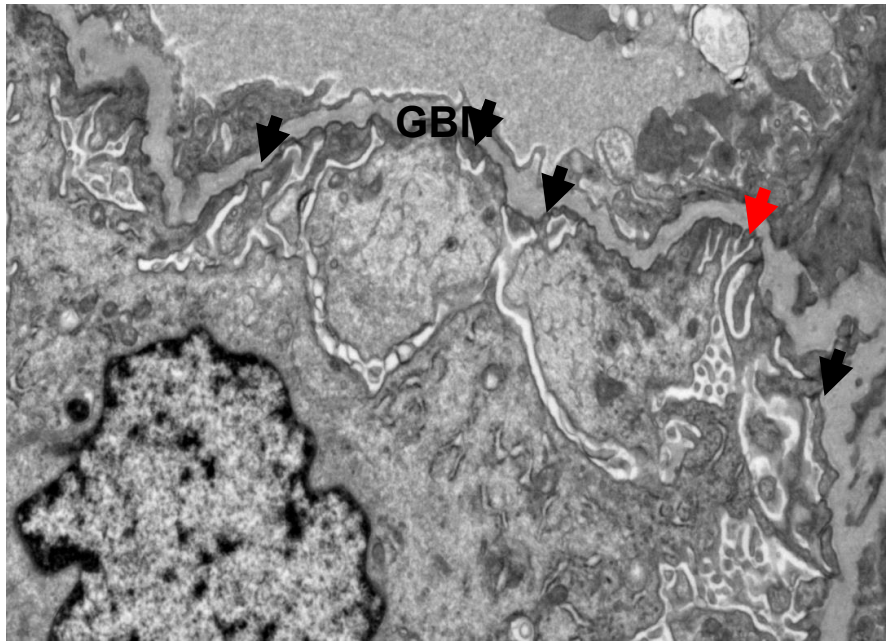
ELX-02 treatment reduced foot process effacement

Kidney morphology improved with less podocyte foot process effacement observed in TEM images of all treated patients

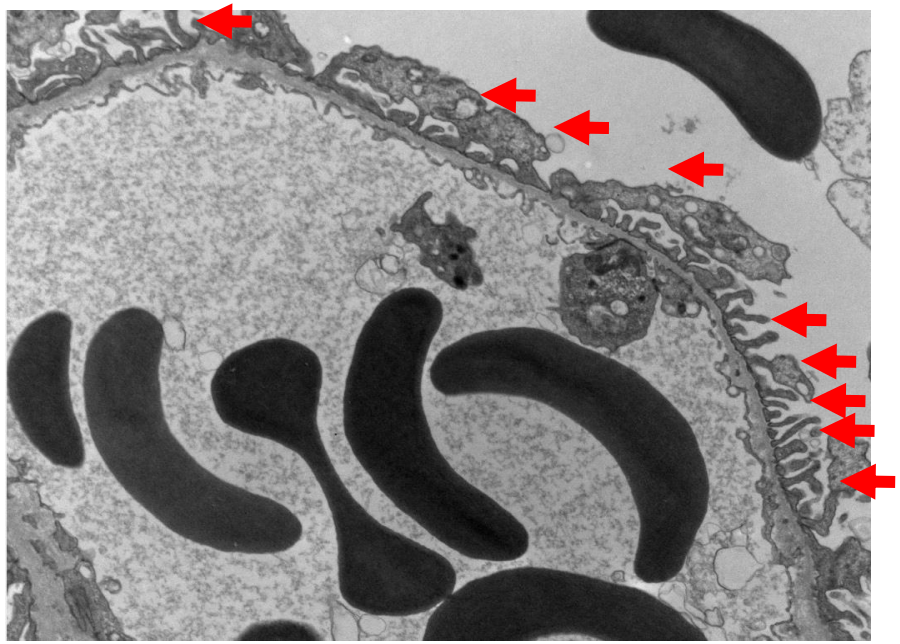
= foot process

= effaced foot process

Pre-treatment: Representative image showing podocyte foot process effacement



Post-treatment (Day 60): Representative image showing intact foot processes



Original assessment by Mayo Clinic validated and quantified by Dr. Behzad Najafian at Univ Of Washington (leading kidney pathologist and TEM expert)

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

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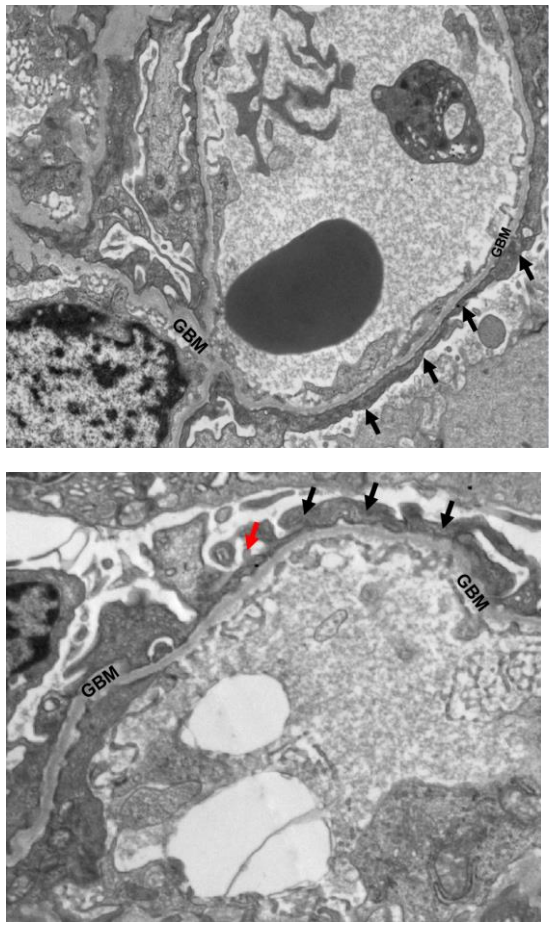
Significant podocyte foot process effacement in all three patients prior to study start

Pre-Treatment representative TEM images

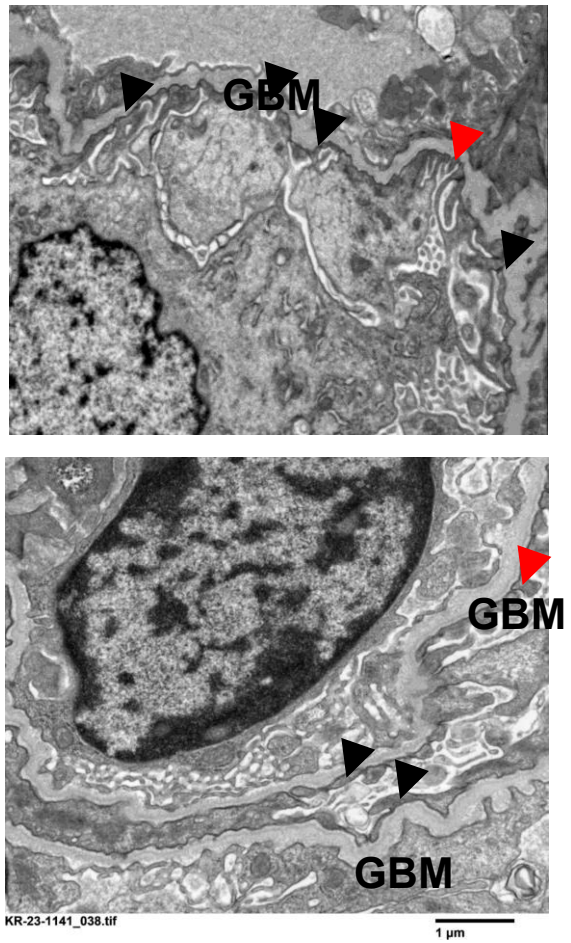
= foot process

= effaced foot process

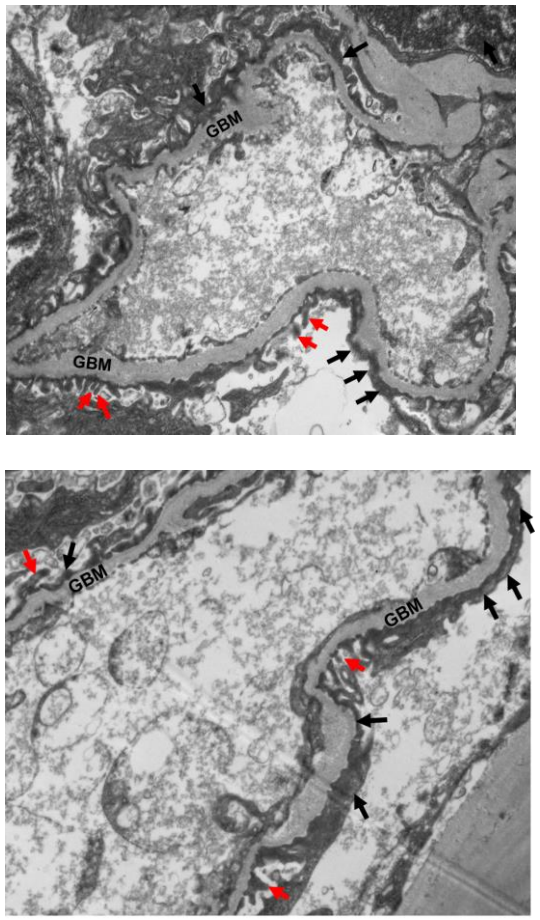
Patient 4401-01



Patient 4401-02



Patient 4402-01



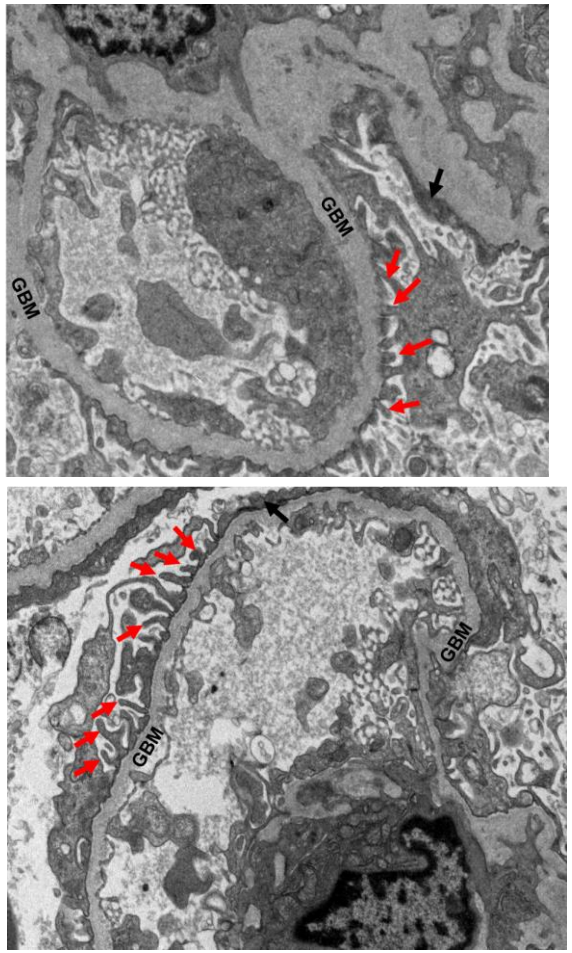
Meaningful reduction in podocyte foot process effacement in all three patients at end of treatment

Post-Treatment representative TEM images

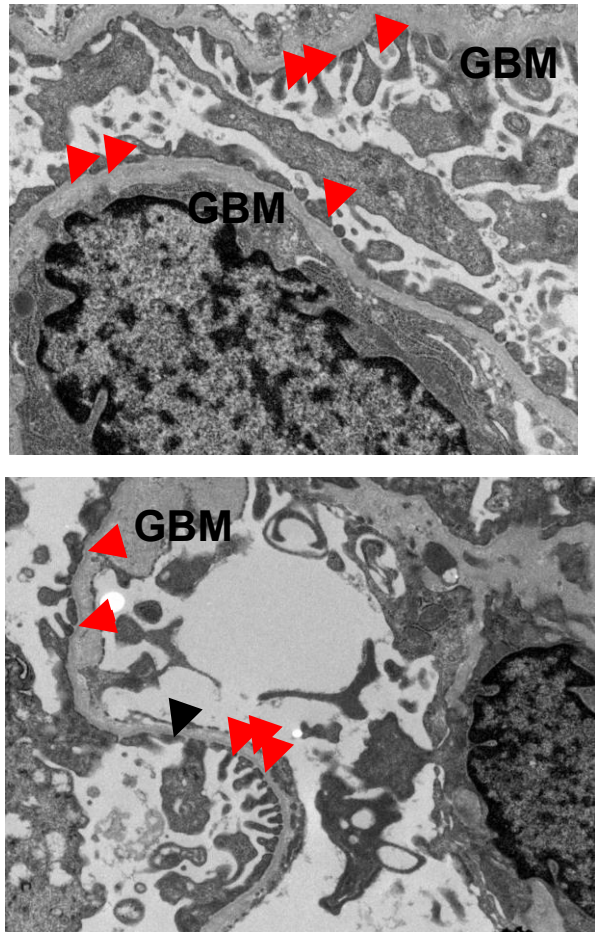
= foot process

= effaced foot process

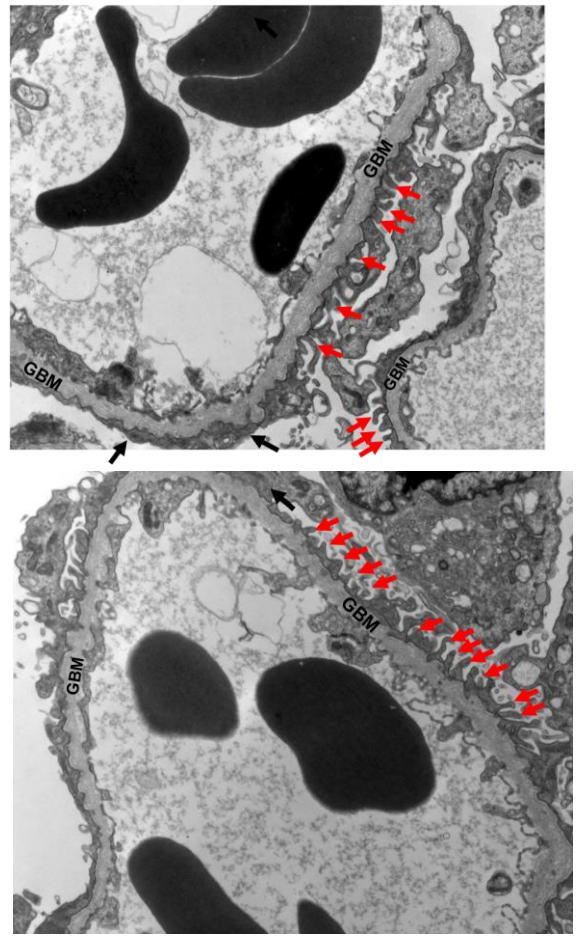
Patient 4401-01



Patient 4401-02



Patient 4402-01



Quantified reduction in Foot process Width (FPW) and increase in Filtration Slit Density (FSD)

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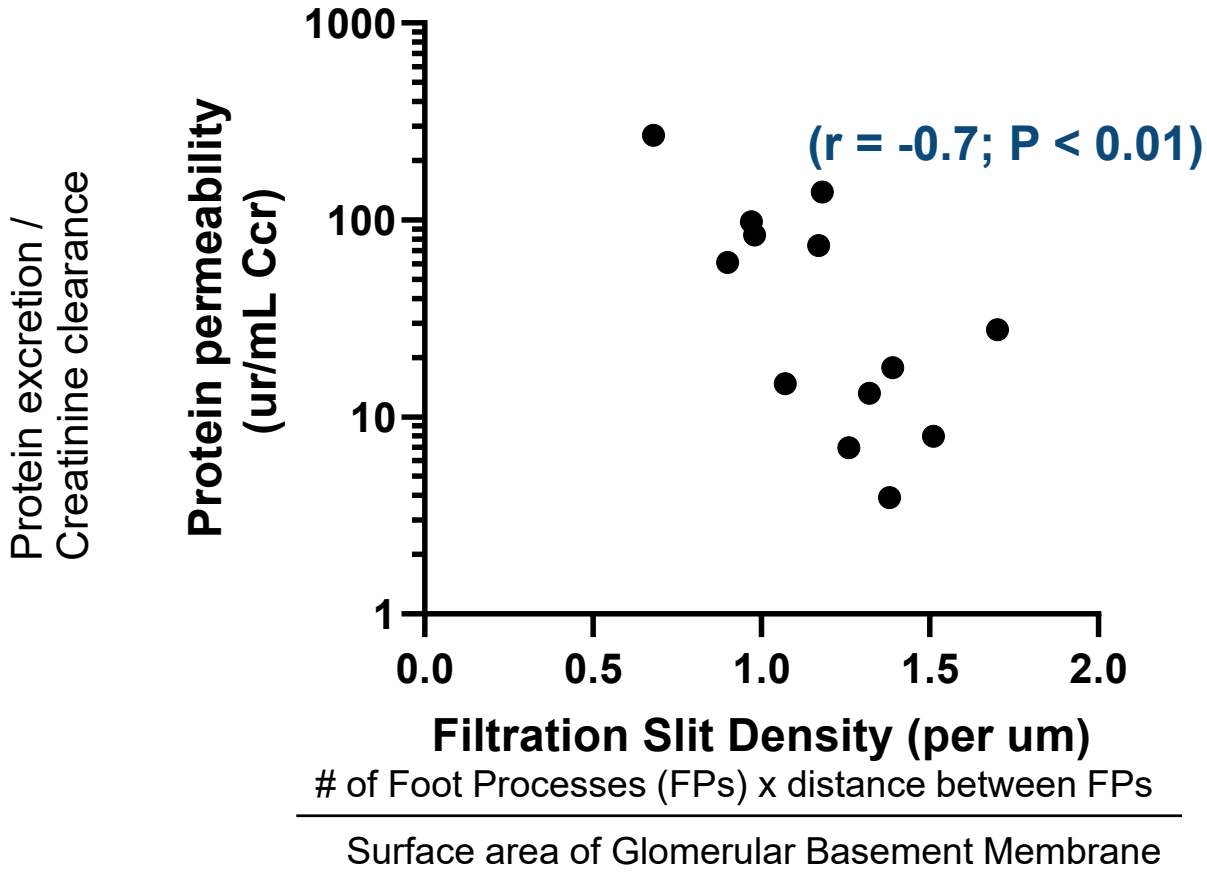
FSD quantified using FPW correlates with degree of proteinuria in Alport

Higher FSD/Lower FPW based on lower Foot process width in TEM images from Alport patient biopsies correlates with lower proteinuria[1]



[1] Kim et al J. Am. Soc. Nephrol. 1995; 5: 1659-1668; Data replotted from Kim et al. Age ranges 4- 26 years. FSD assessment using Light microscopy and TEM image analysis of kidney biopsies

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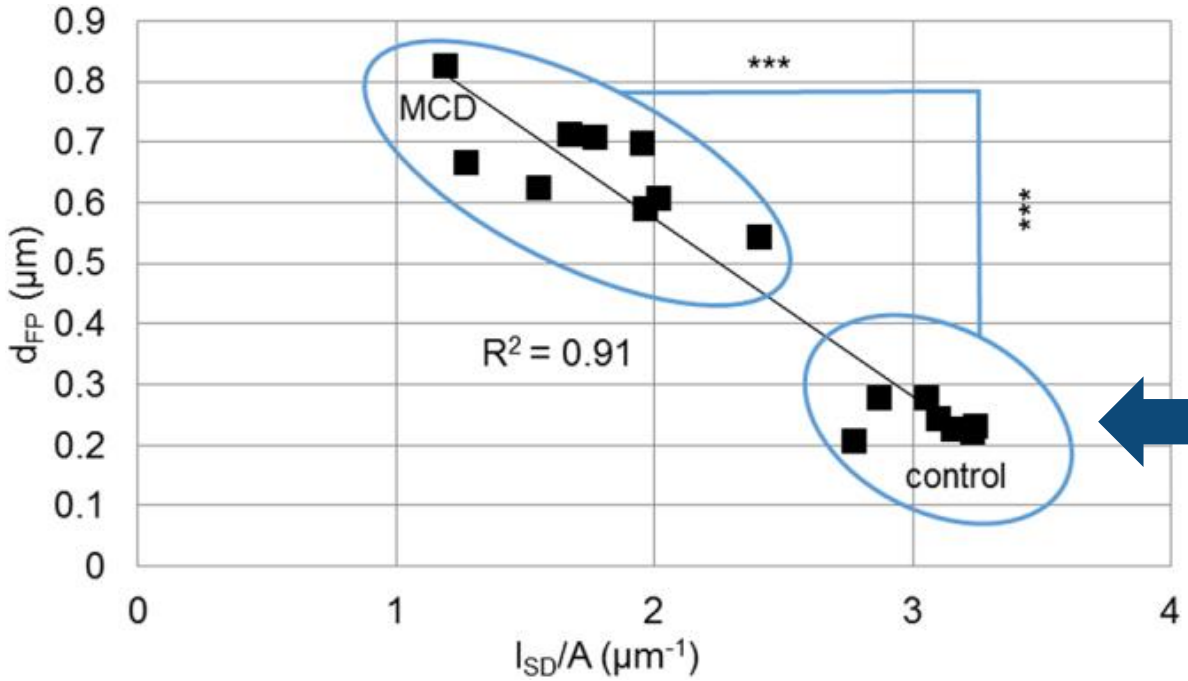
New more robust assay for estimating FSD from FFPE biopsies provides accurate and unbiased results

Nipoka labs has developed a highly automated, unbiased and accurate assessment of filtration slit density than TEM based FSD/FPW[1]

Foot Process width estimated from patient TEM biopsies



Filtration Slit Density estimated from patient Formalin Fixed Paraffin Embedded (FFPE) biopsies by Nipoka[2]

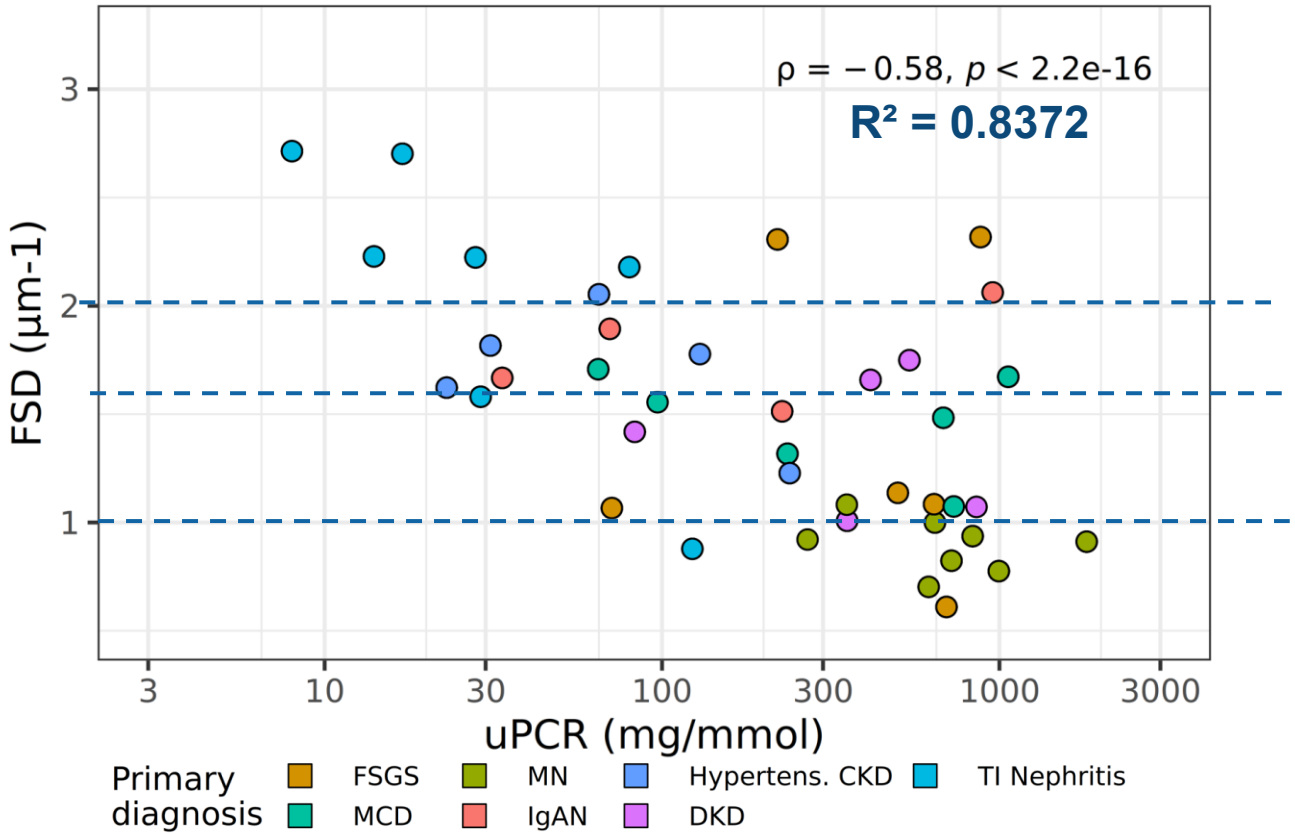
Healthy FSD: 3.10 ± 0.27 µm−1

[1] Mean values of d_{FP} (Foot process width) and I_{SD}/A measured in biopsies of either Minimal Change Disease or (MCD)control subjects, are plotted against each other for each individual. There is a significant difference between the MCD and the control group for both d_{FP} and I_{SD}/A ($p < 0.001$, Mann-Whitney U test); Adapted from Siegerist 2017

[2] FFPE Biopsy samples immunostaining for foot-process specific protein markers followed by 3D-SIM imaging to quantify Filtration Slit Density (FSD) per glomeruli and averaged across 15-20 glomeruli. Normal Patients have an FSD of approx. 3.0. This analysis has been validated in multiple glomerular diseases

Glomerular diseases with higher proteinuria associated with lower FSD

FSD estimated by NIPOKA in 69 patient biopsies from NURTuRE prospectively assessed correlated with proteinuria[1,2]



FSD>2: Highly significant reduction in effacement

FSD>1.6 Clinically meaningful improvement

FSD<1: Highly diseased

[1] Taal MW et al.: Associations with age and glomerular filtration rate in a referred population with chronic kidney disease: Methods and baseline data from a UK multicentre cohort study (NURTuRE-CKD). Nephrol Dial Transplant 10.1093/ndt/gfad110

[2] Abstract: TH-PO786, ASN 2023

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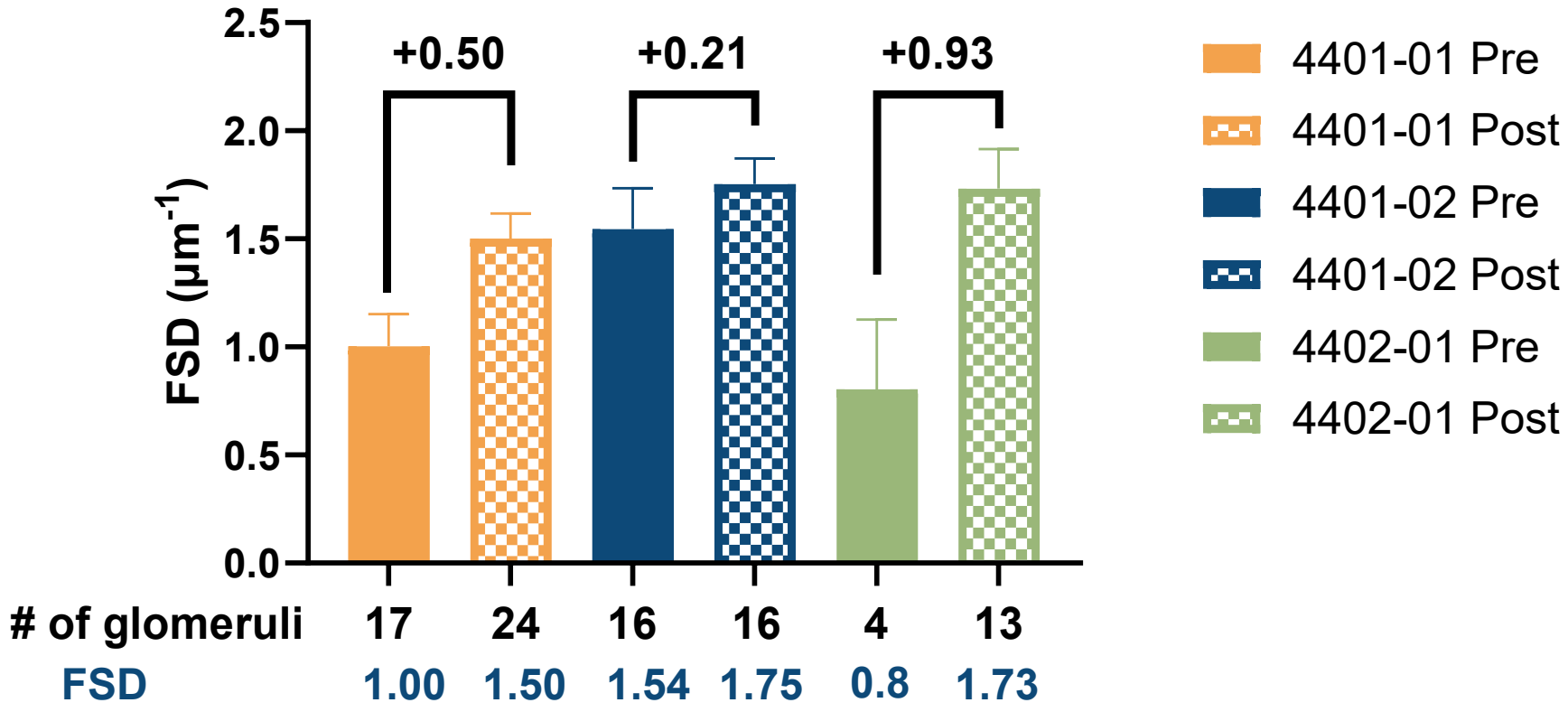
Change in FSD exceeded minimal threshold for meaningful reduction in foot process effacement of FSD ≥0.15

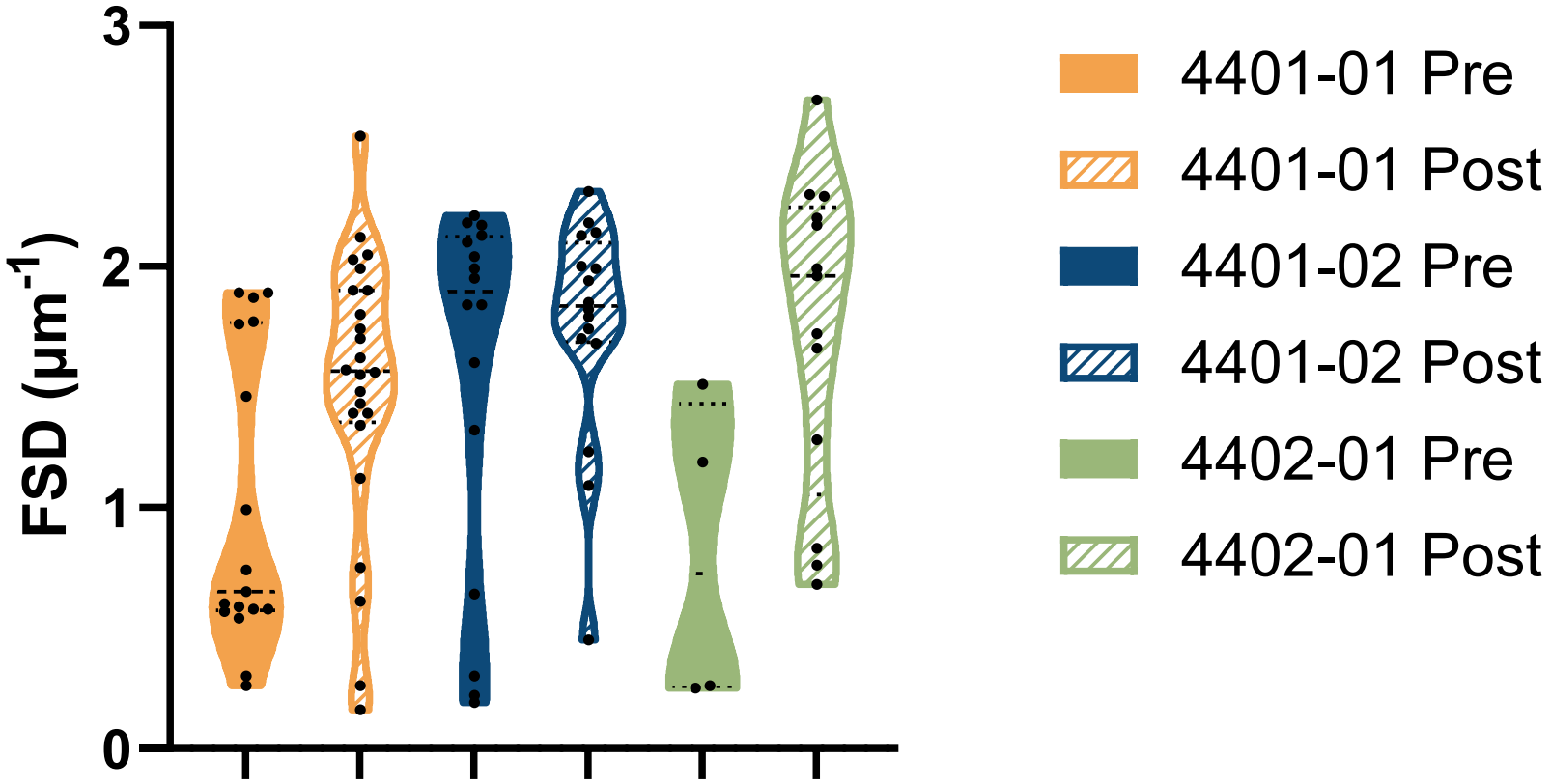
Improvement in FSD* is an independent confirmation of collagen IV expression and foot process effacement and predicts clinical benefit



*Slit diaphragms are stained with podocin and podocyte foot processes labeled by synaptopodin. Filtration slit density (FSD) is calculated by dividing the length of the slit diaphragm by the area covered by podocyte foot processes using 19 optical sections in each glomerulus.

Clear shift towards healthy FSD levels in all Alport patients and the end of treatment with ELX-02

FSD values for single glomerulus further reinforces treatment benefit with ELX-02 as distribution of glomeruli with an FSD >1.5 increase in all patients



Clinically meaningful reduction in UPCR in 2 patients consistent with absolute level of FSD

UPCR improvement consistent with morphology improvement since spontaneous reduction is not possible due to lack of Collagen IV protein

Patient	Baseline	UPCR average during treatment period	UPCR at end of treatment (EOT 8 weeks)	Average UPCR 8 weeks post treatment	Baseline vs. EOT FSD
4401-01	1299.5 ± 395.1	1882 ± 830.9	2465.7 ± 1340	1929.9 ± 270.4	1.0/1.54
4401-02	1646.3 ± 334.5	850 ± 308.5* -48.4%	1028.1 ± 528.9 -37.6%	1680.3 ± 179.8	1.5/1.75
4402-01	1645.3 ± 391.6	2209 ± 913.4	2634.7 ± 491.4	1236.7 ± 161.4 -25%	0.8/1.73

≥30% reduction in UPCR is validated as a predictor of improved renal outcomes
Blood pressure and eGFR stable during treatment and no tubular damage during treatment

* Excludes Week 6 UPCR values based on recommendation of principal investigator. UPCR declined by 30% even when including week 6 for patient 4401-02

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Strong support by Alport community of treating clinicians, KOLs, and patient advocates to proceed

- Significant KOL conviction in potential of ELX-02 based on data
  - Results consistent with studies of protein restoration in Alport knockout mice (Jeff Miner, Alport Syndrome Foundation (ASF) scientific advisory board member)
  - Changes in biopsy consistent with activation of signaling pathways
  - UPCR reduction in just 2 months considered impressive given hemodynamic variability
- Confirmed interest in clinical trial participation by treating clinicians
  - 13 clinicians in US and Ex-US reviewed data and want to participate
  - Several Physicians on ASF medical advisory board (e.g., Dr. Michelle Rheault, Dr. Alessia Fornoni, Dr. Rasheed Gbadegsein and Dr. Moumita Barua)
  - Physicians in UK and Australia have identified 12 potential patients
- Data presented by Dr. Michelle Rheault at ASN in November on her own request
- Strong support from Alport Syndrome Foundation: “The AS community needs this to happen”

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Planning global pivotal registration trial

- Pivotal registration study plan contemplates clinical sites in US, UK and Europe
- Eloxx is positioned to execute clinical study
  - Substantial clinical experience with ELX-02, with two open INDs with FDA and studies completed (CF, cystinosis, Phase 2 in Alport Syndrome)
  - **Key safety risk has been discharged in human subjects**
  - Strong CMC position, we know how to manufacture DS and DP, current inventory available (4904 vials available, 3,225 needed)
- Regulatory plans
  - Orphan Drug Designation (received in April 2024)
  - In-person Pre-IND meeting in the US scheduled
  - Seek Orphan Drug Designation in Europe, UK
  - Seek regulatory approvals to start pivotal trial in the UK

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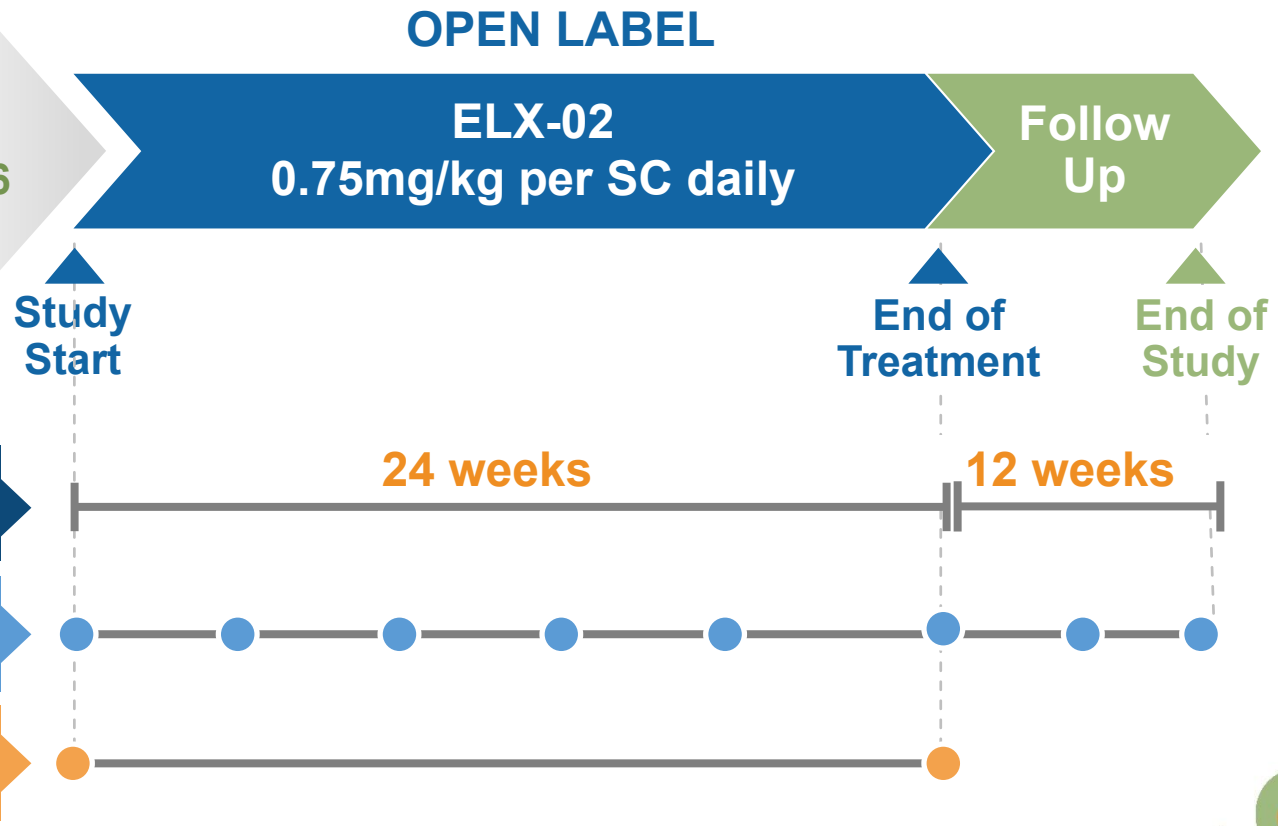
Proposed ELX-02 Phase 2/3 trial consistent with POC trial with longer duration to serve as potential registrational study

Inclusion Parameters	Criteria
Genotype	Any patient with nonsense mutations in the *COL4A3/4/5* gene except UAA stop codon
Age	All patients ≥12 years
eGFR	≥45ml/min/1.73m^2 BSA
Proteinuria	≥300mg/g

n= 16



Study design guided by Phase 2 results and advice from network of clinical advisors

Alport Pivotal Study Design (1/2)

Trial design	
Control	**Open label** • *Unethical given Phase 2 results and rare patient population* • *Endpoints are objective and allow each patient to be their own control*
Number of patients	16 to 20 (US, UK, Europe); • *Assumes at least 35% patients have a ≥25% reduction in UPCR and an FSD change of ≥0.2*
Number of countries/sites	UK: 4 - 6; US(8 – 12); Europe (TBD)
Treatment duration	24 weeks dosing ELX-02 SC 0.75mg/kg/day on top of maximal tolerated RAASi + 12 weeks follow up

Inclusion criteria	• X-linked (COL4A5) male or Autosomal recessive(COL4A3/A4) Alport patients with Nonsense mutations
	• eGFR≥45
	  • *CKD Stage ≥3a likely to have sufficiently preserved number of podocytes*
	• UPCR≥300mg/g
	  • *Guidance for Alport trials*
	• ≥12 years old (6-11 year olds may be included after safety review)

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Co-primary efficacy endpoints of FSD and UPCR change supported by Phase 2 results and FDA guidance

Alport Pivotal Study Design (2/2)

Trial design	
Primary safety endpoint	• Percentage of patients with Serious Adverse Events (SAEs) • Percentage of patients with treatment-emergent Adverse Events of Special Interest (AESIs)

Primary efficacy endpoints	• Change in FSD at end of treatment compared to pre-treatment biopsies.
	  • *Objective, unbiased and quantitative measure of foot process effacement*
	• Change in UPCR at end of treatment (24 weeks) and at 12 weeks of follow up (36 weeks) compared to baseline
	  • *UPCR change is an acceptable end point for full or accelerated approval in glomerular disease (per FDA cardiorenal division)*
	  • *Median UPCR of patients with eGFR 30 is 1900mg/g*

Key Secondary efficacy endpoints	• Qualitative assessment of podocyte foot process effacement from TEM images
	• Change in Foot Process Width (FPW) based on deep learning methodology
	  • *Has been submitted as potential biomarker to FDA*
	• Change in UACR at end of treatment (24 weeks) and at 12 weeks of follow up (36 weeks)
	  • *Alternative measure of kidney function, correlated to UPCR*

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ELX-02 provides significant optionality

- Near term regulatory milestones: Orphan Drug Designation and pre-IND meeting, Phase 3 start
- Increased strategic interest in rare diseases and including kidney
  - Chinook acquisition by Novartis
  - Otsuka has >$800M ADPKD franchise
  - Astra Zeneca focused on building rare disease franchise with Alexion acquisition
  - Vertex: Phase 3 program in genetic APOL1 mediated kidney diseases
  - Multiple gene therapies with programs overlapping with Eloxx (e.g., Vertex, 4D Molecular, Sarepta, etc.)
  - Strong interest in RNA biology
- Potential Genzyme/Gaucher disease type of opportunity and path to commercialization

  Estimated prevalence, pricing, profitability:
  - US: prevalence- 7,500; Pricing: $600K
  - Ex US developed: Prevalence- 10,000; Pricing: $400K
- Eligible for PRV on approval (~$100 million estimated value); last deal done at $103 million

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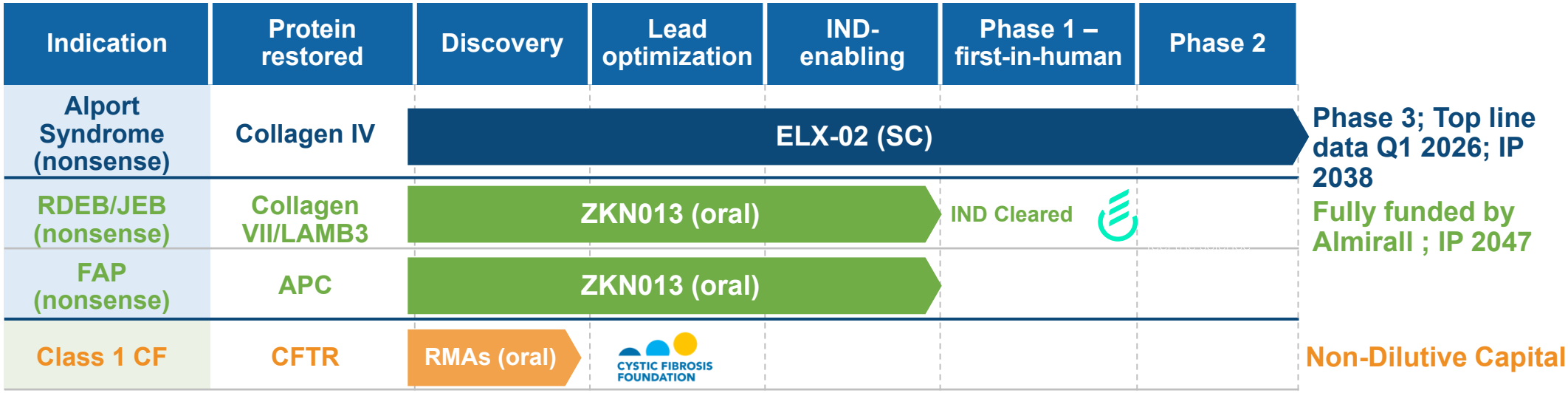
Appendix

Lead renal program positioned for commercialization by 2027 with second program partnered with Almirall



Class 1 CF: Cystic fibrosis patients with class1 mutations; **RDEB/JEB:** Recessive Dystrophic/Junctional Epidermolysis Bullosa; **FAP**: Familial adenomatous polyposis

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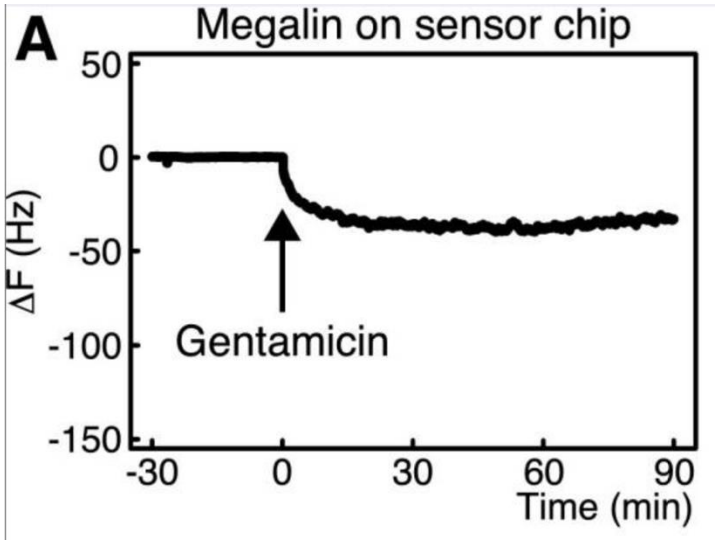
ELX-02 uptake by megalin in the kidney expands therapeutic index

Aminoglycosides are taken up megalin present in the kidney, inner ear and eyes

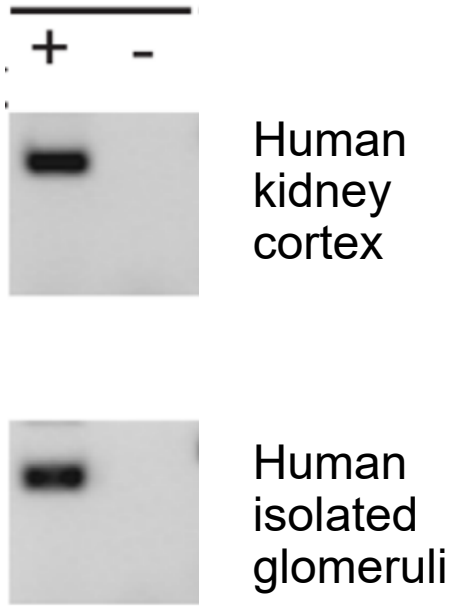
Megalin binding of aminoglycosides[1]

Quartz Crystal Microbalance experiment[1]

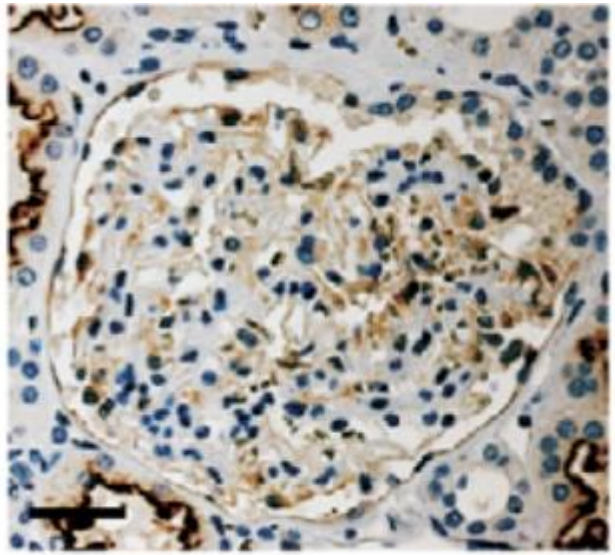


RNA levels for megalin in kidney (RT-PCR)[2]

Reverse transcriptase



Immunohistochemistry* for megalin in Glomeruli[2]



[1] J Am Soc Nephrolv.28(6); 2017 JunPMC5461786
[2] PLoS ONE 6(9): e25065. doi:10.1371/journal.pone.0025065
*DAB staining

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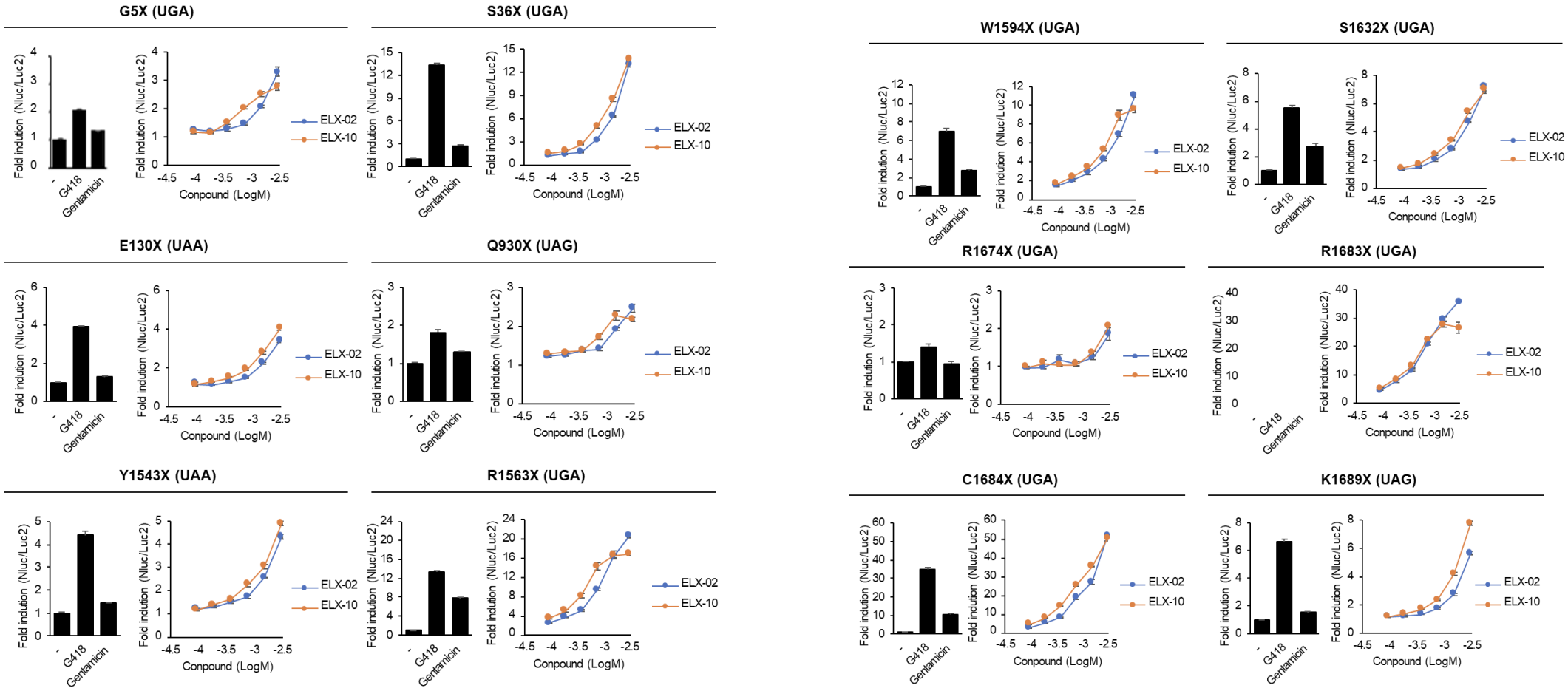
ELX-02 induces significant full length collagen IV across nonsense COL4A5 mutations

ELX-02 readthrough COL4A5 nonsense mutation in HEK293 cells at 24 hours resulted in 6 to 15% full-length collagen IV protein induction



Experiment conducted at Washington University by Dr. Jeff Miner, Poster Presentation at ASN 2022 “Investigational therapy of Alport Syndrome with ELX-02” Hariri, Omachi, Miner et al

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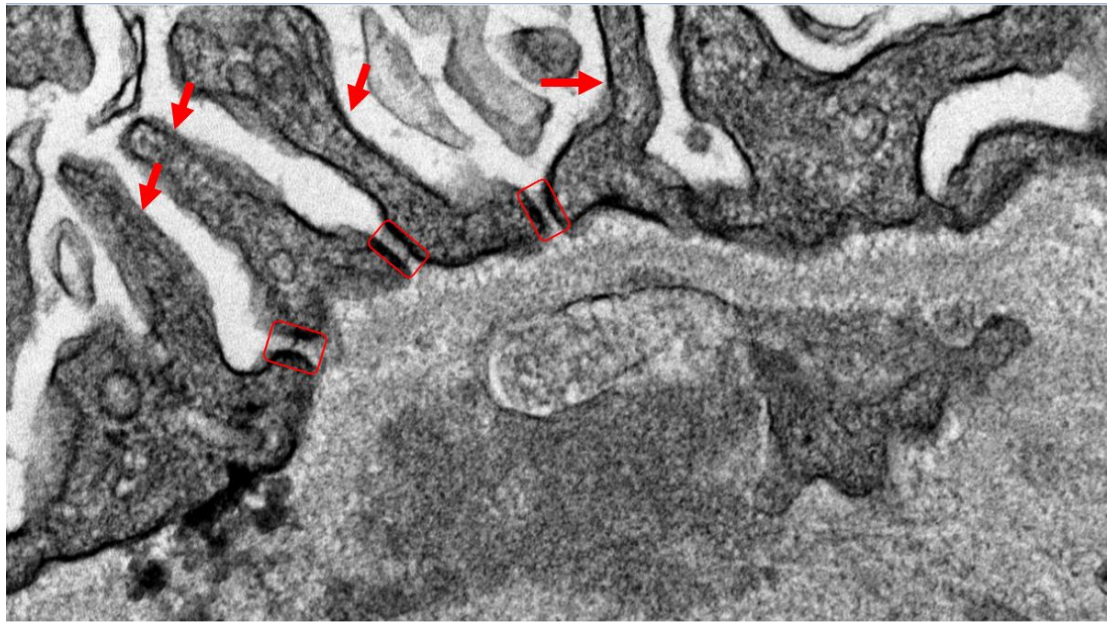
Changes confirmed by reduction of foot process width (FPW) and increase in filtration slit density (FSD)

Unbiased and blinded quantification of foot processes by Dr. Najafian

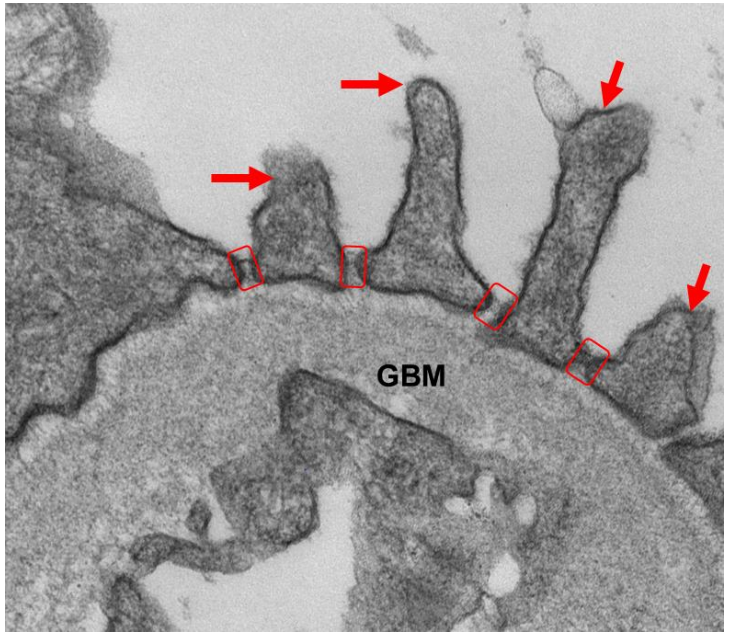
= slit diaphragm

= foot process

Patient 4401-01 (day 60): -19% reduction in Foot Process Width



Patient 4402-01 (day 60) : -45% reduction in Foot Process Width



Improvement in podocyte foot process architecture consistent with the MoA of ELX-02 to restore full length COL4A4 resulting in re-expression of collagen α3/α4/α5 (IV) trimer in the GBM

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

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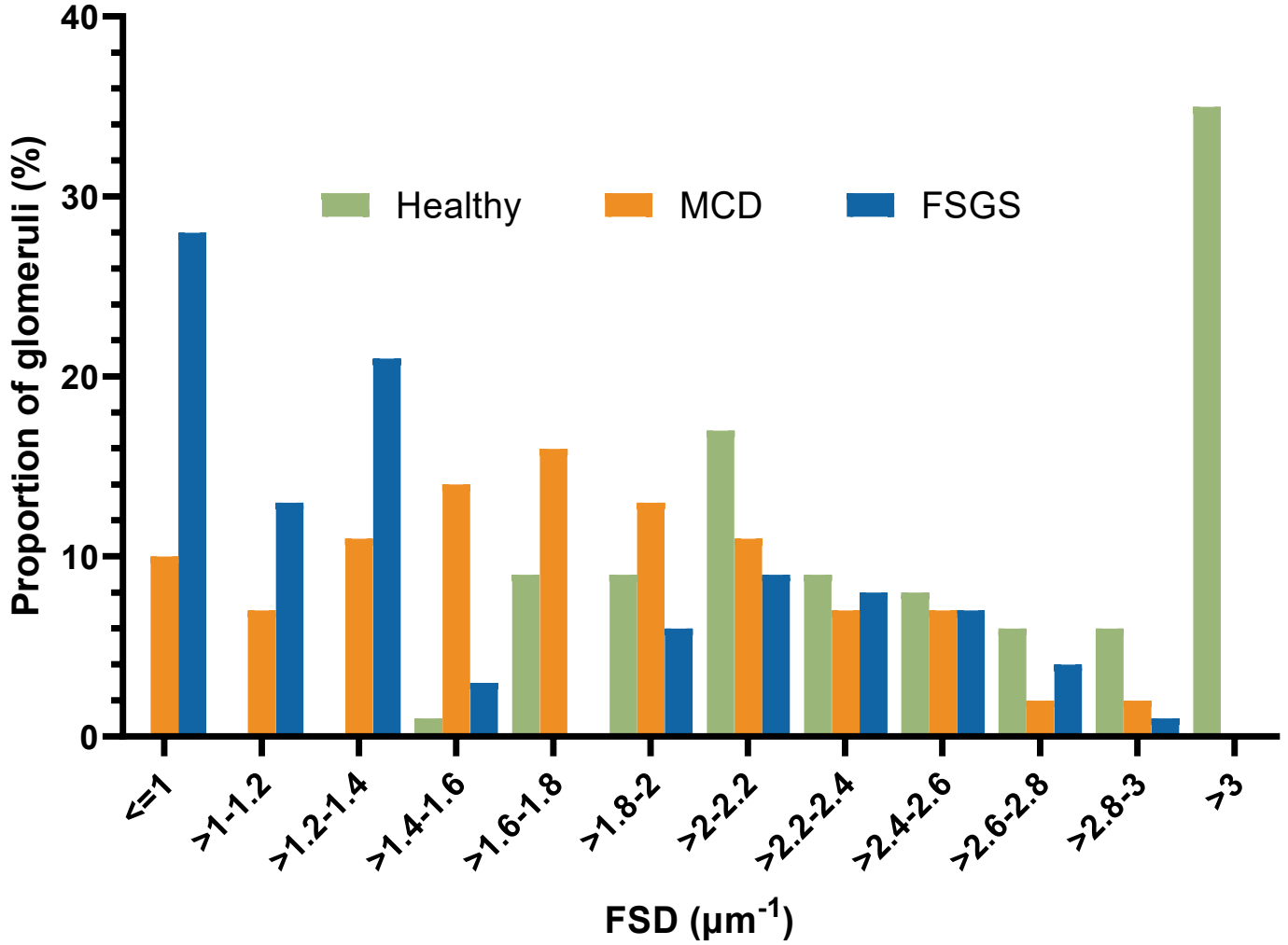
Distribution of FSD skewed to lower FSD (<1.2) in patients compared to controls

Distribution of Glomeruli by FSD for Patients Compared to Controls*



NIPOKA

Shifts as low as 0.1 to 0.3μm^{-1} can be predictive of a change in Foot Process Effacement

246 glomeruli from 17 healthy volunteers; 236 glomeruli from 23 MCD patients; 122 glomeruli from 12 FSGS patients. Data from Siegerist et al. (2017) and NURTuRE CKD cohort analysis.

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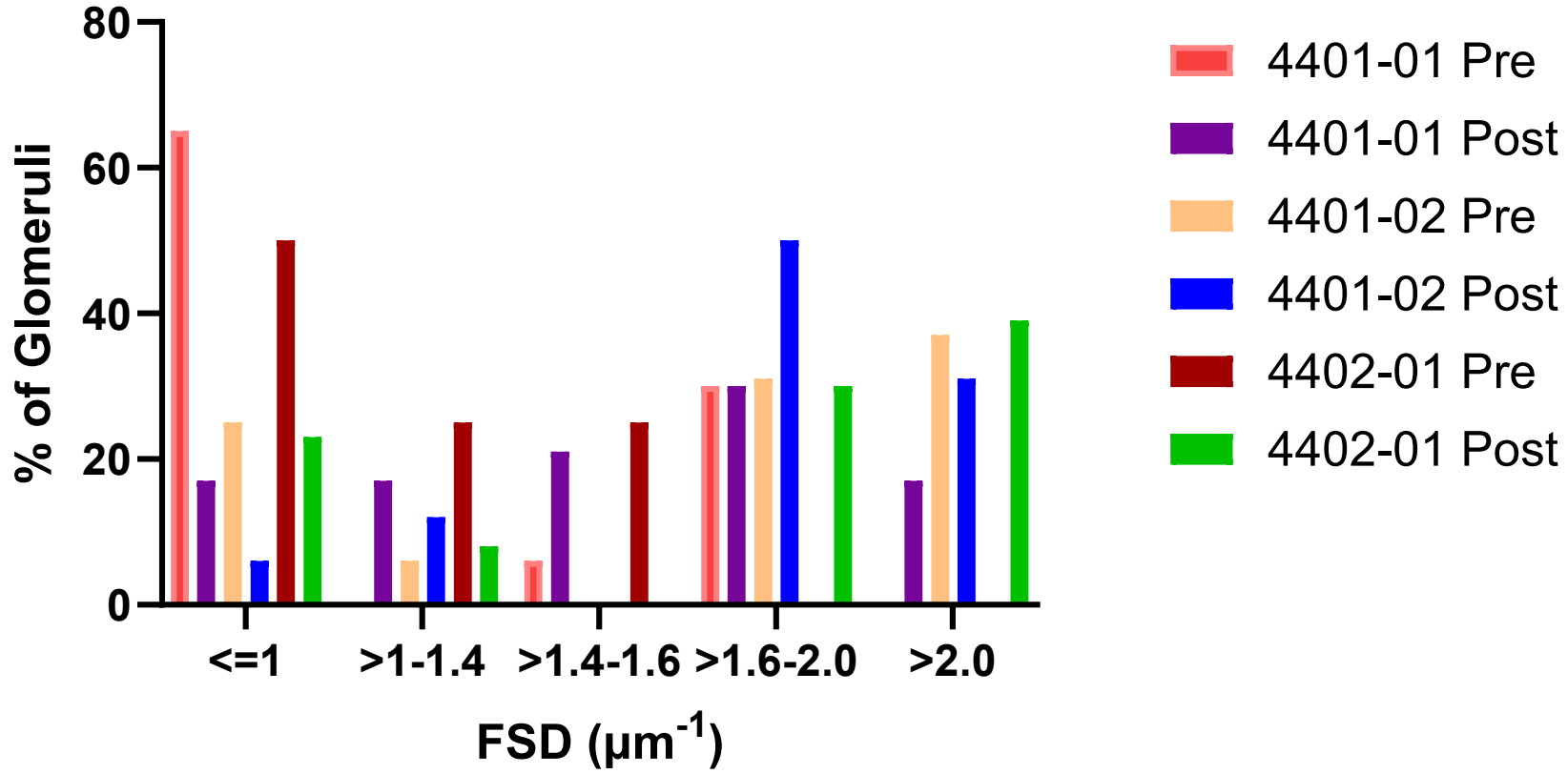
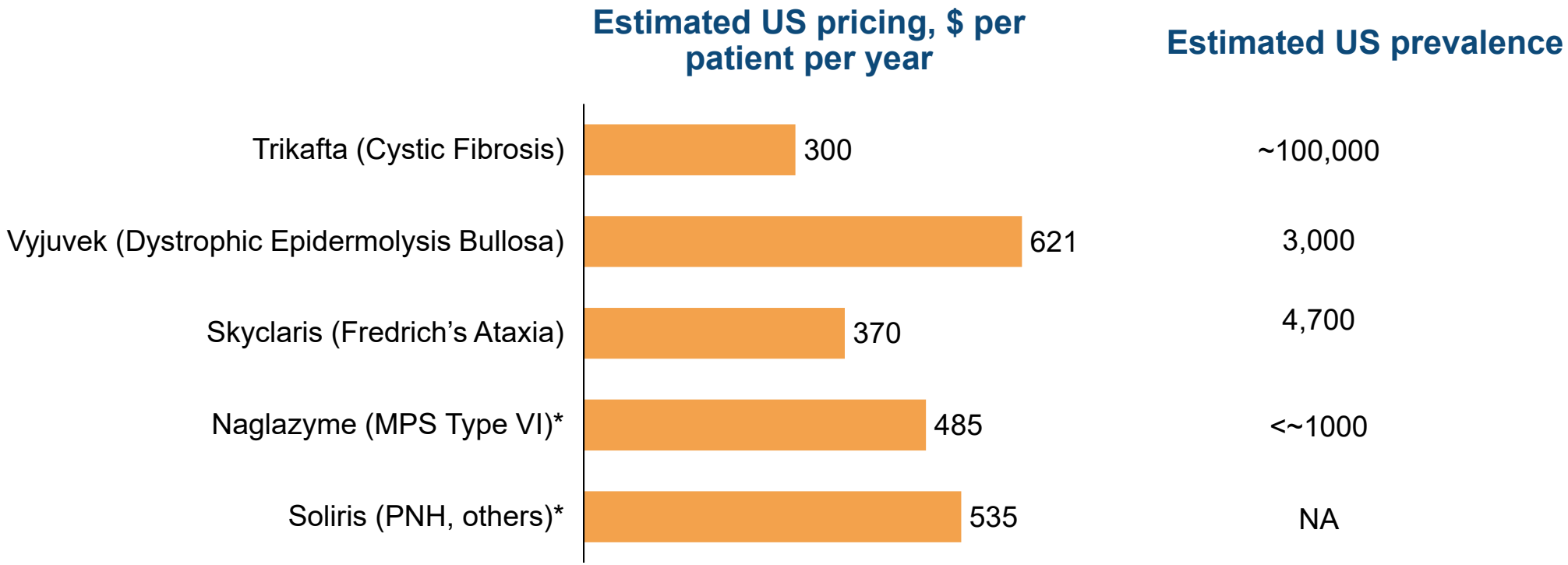
Significant decrease in proportion of FSD values <1 indicating consistent with shift to moderate/segmental effacement

FSD distribution across glomeruli at end of treatment compared to baseline



ELX-02 and ZKN-013 profiles support rare disease drug pricing

ELX-02 and ZKN-013 expected to be priced similar to other disease modifying rare and orphan drug therapies in the US



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Three alport phase 2 studies active evaluating non-disease modifying therapies

Study Name	Drug Name	MOA	Control	Trial size	Duration (weeks)	Age	UACR / UPCR	eGFR	Efficacy endpoint
ALPESTRIA-1	vonafexor	Anti fibrotic: Highly selective FXR agonist	Open label	20 (3 dose cohorts)	24	16-40	n/a	n/a	n/a
R3R01 - ASFFSGS - 201	R3-R01	Reduce the accumulation of toxic lipids in podocytes	Open Label	20	12	18+ (12+ ex US)	UPCR ≥ 1.0 g/g	≥ 45 mL/min/1.73 m2	Change in UPCR
Setanaxib/ Calliditas	Setanaxib	NOX inhibitor – anti fibrotic/anti inflammatory	Placebo	18	24	12-40	UPCR ≥ 0.8 g/g	≥30 ml/min/1.73 m2	% of patients with 25% reductio in UPCR, Change in UPCR vs baseline

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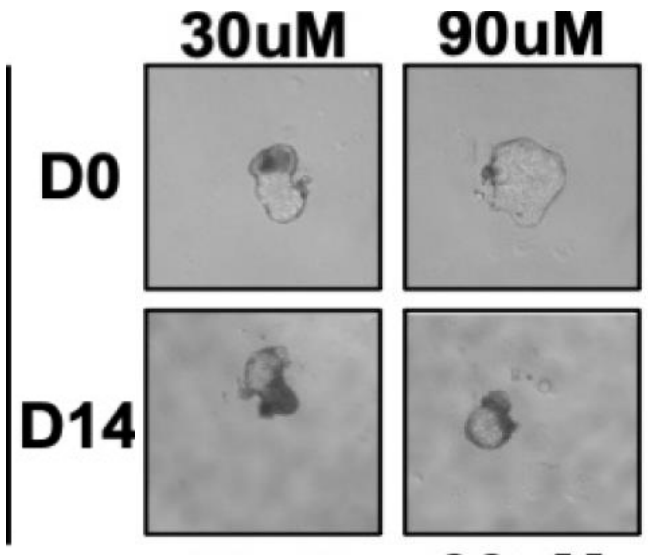
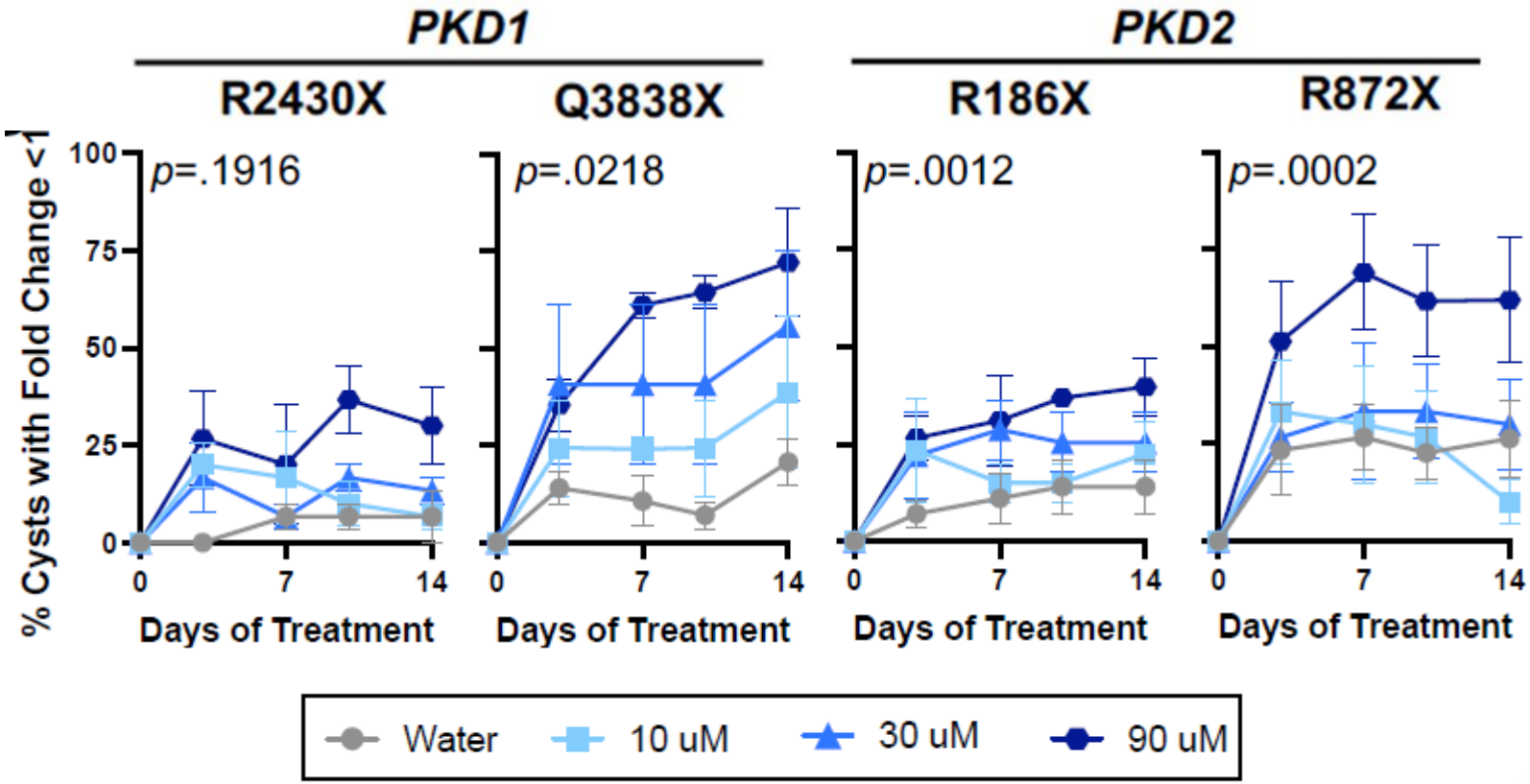
Alport results support expansion into ADPKD

ELX-02 has shown cyst number and size decline in 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.

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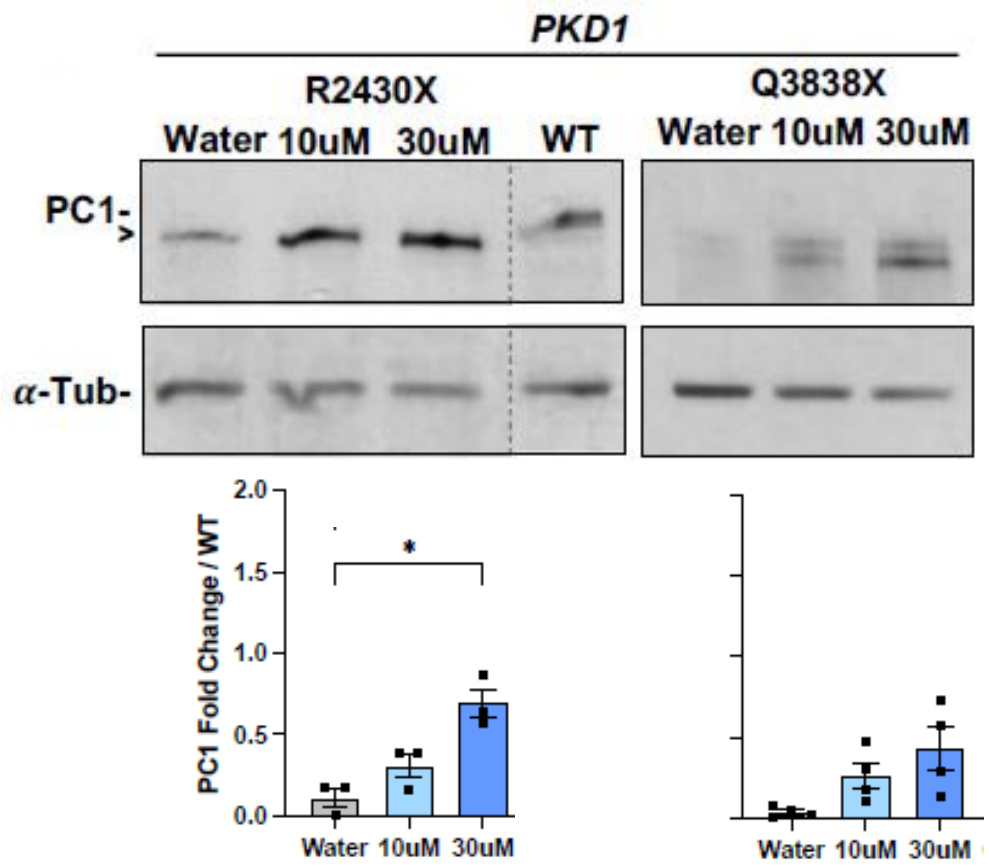
ELX-02 treatment of ADPKD kidney organoids results in increase PKD1 protein levels

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

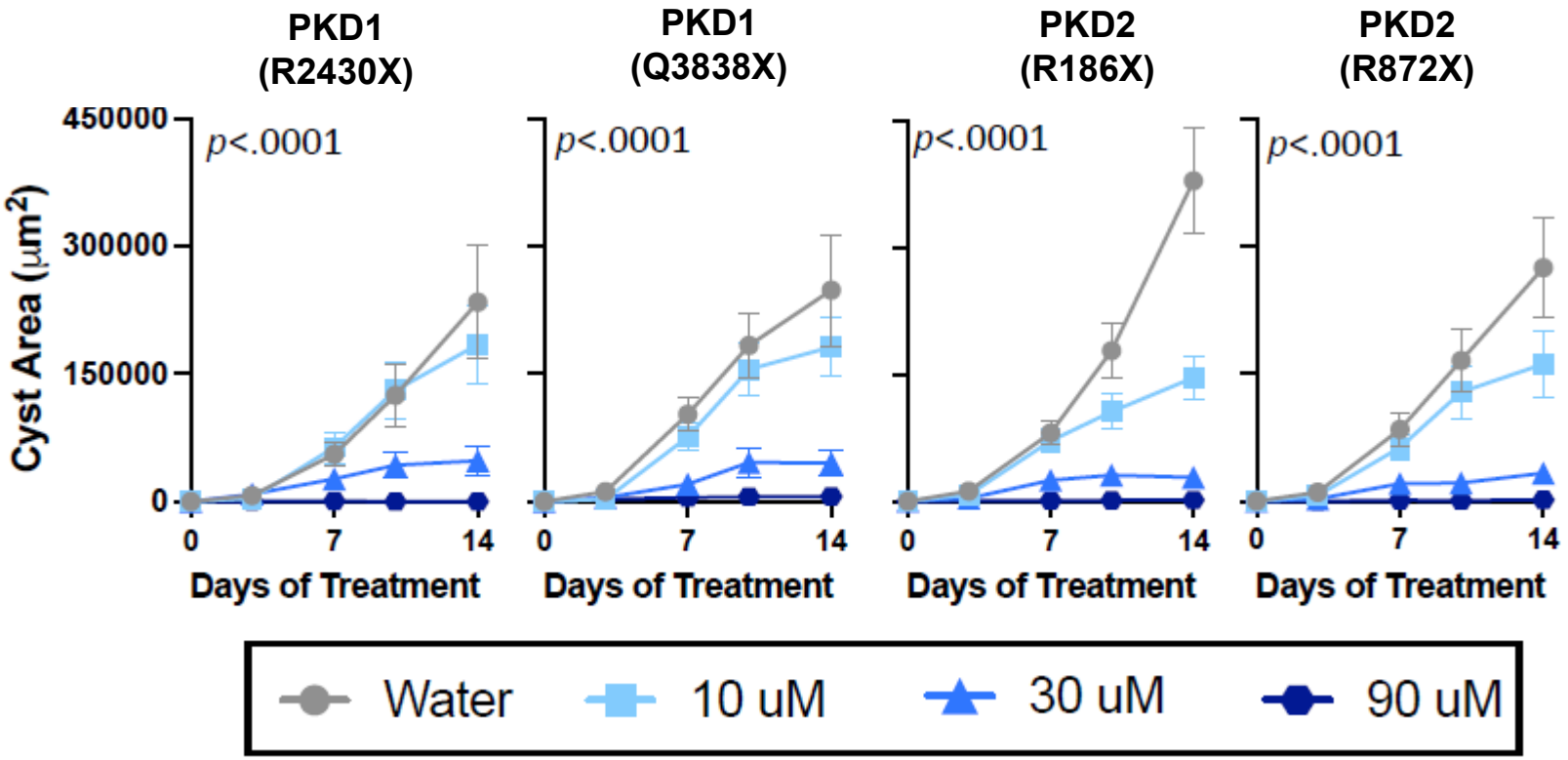


*Data generated in collaboration with Freedman lab at University of Washington.

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.

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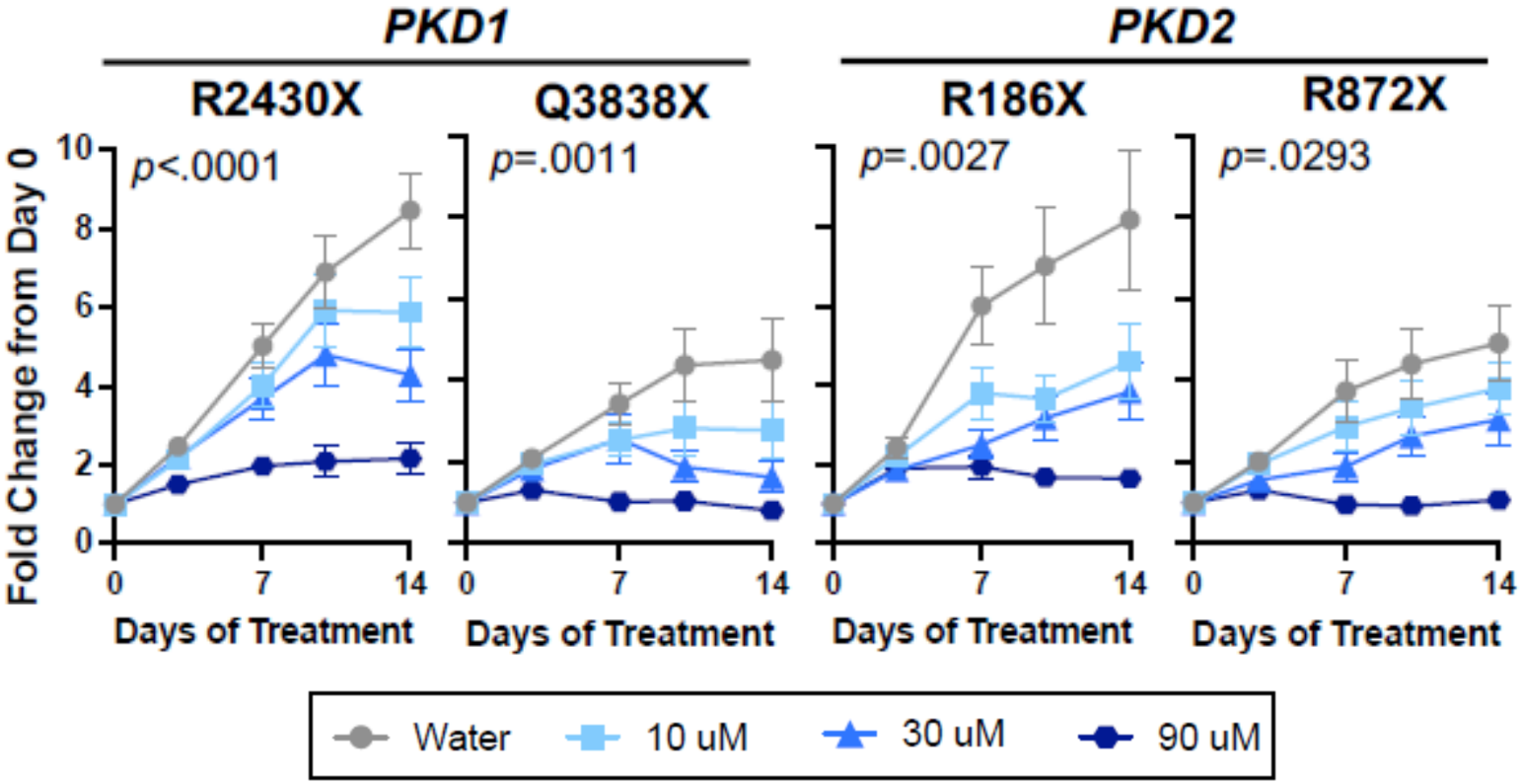
ELX-02 treatment of ADPKD kidney organoids inhibits growth of pre-existing cysts

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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