Eloxx Pharmaceuticals

Unlocking protein production with **translational read-through** for **rare genetic** diseases

Investor Presentation

January 2020

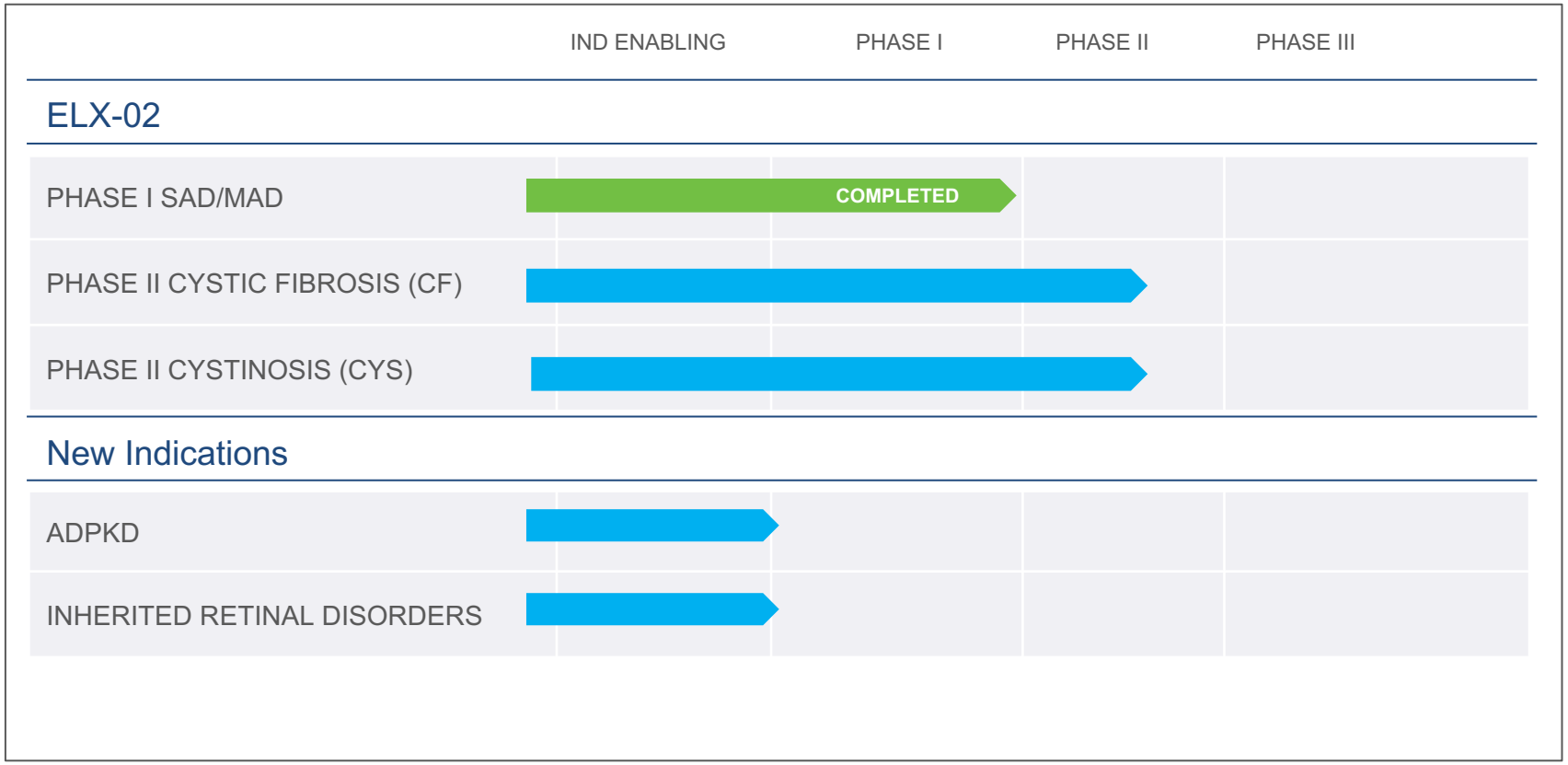
Forward-Looking Statements

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 read-through 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; 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 Pharmaceutical Highlights

- **Experienced Leadership Team**
- **Phase 2 Cystic Fibrosis Top Line in 1H 2020**
  - **A Phase 2 Study to Evaluate the Safety, Tolerability, PK and PD of ELX-02 in Cystic Fibrosis Patients With G542X Allele**
  - **Dosing underway, on target for full enrollment 1Q**
    - **US Trial** NCT04135495
    - **EU/IL Trial** NCT04126473
- **Phase 2 Cystinosis Top Line Results 1st Cohort**
  - **First cohort complete, SRC greenlight for initiation of second cohort**
  - **Demonstration of biologic activity for ELX-02 with acceptable safety/tolerability**
- **Pipeline Development: ADPKD, Ocular Inherited Retinal Disorders**
  - **ADPKD in vitro read through screening on highest prevalence nonsense mutations complete**
  - **Ocular Oca2 animal model shows POC for intravitreal administration, sustained release underway**
  - **New Ocular data to be presented at the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting May 3-5, 2020 Baltimore, MD**
- **Actively Developing Business Development Opportunities to Advance Full Pipeline and Expand Therapeutic Programs**

Eloxx Pipeline
Phase 2 in Cystic Fibrosis and Cystinosis



ELX-02: Phase 1 Program Completed

SAD (single ascending dose)

- ✓ Submission of CSR to regulators
- ✓ Published in *Clin. Pharm. Drug Dev*. 2019 Jan 16.
- ✓ PK presented at ECFS 2019
- ✓ **Full data presented at NACFC Oct. 31- Nov. 2, 2019**

MAD (multiple ascending dose)

- ✓ **Full data presented at NACFC Oct/Nov 2019**
- **CSR and manuscript to follow**

Renal Impairment

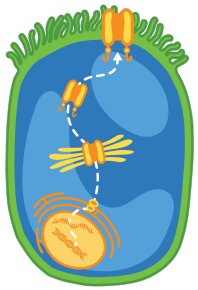
- ✓ **Full data presented at ASN Kidney Week Nov. 5-10, 2019**
- **CSR and manuscript to follow**

Phase 1 Program Conclusions

- Generally well tolerated in clinical studies to date supporting evaluation in Phase 2
- Consistent PK results across single and multiple dose studies, with no accumulation
- High bioavailability (98%) upon SC administration with highly reproducible PK over the dosage range studied (0.3-7.5 mg/kg)

Our Orphan Drug Programs Have Strong Advocacy Support

ELX-02: Preclinical Data De-Risks Phase 2



- ELX-02 is a small molecule that permits read-through of nonsense mutations
  - ✓ High selectivity for the eukaryotic cytoplasmic ribosome relative to mitochondrial ribosome
  - ✓ Defined MOA: Demonstrated significant increases in Cystinosin & CFTR *mRNA*, protein and function
  - ✓ Demonstrated read-through in assays focusing on high prevalence Cystic Fibrosis & Cystinosis nonsense mutations
- ELX-02 high activity in multiple cellular and animal models
  - ✓ Pronounced *CFTR* read-through demonstrated in plasmid, HBE, FRT, transgenic mice and patient-derived organoids
  - ✓ Pronounced Cystinosin read-though demonstrated in plasmid, patient derived fibroblasts and transgenic mice
- Phase 2 Studies enroll patients with defined genotypes
  - Cystic Fibrosis trial focuses on G542X on one or both alleles
  - Cystinosis trial focuses on nonsense mutations, like W138X

ELX-02: Phase 2 CF Top Line in 1H 2020

- **Phase 2 Cystic Fibrosis Program**
  - **A Phase 2 Study to Evaluate the Safety, Tolerability, PK and PD of ELX-02 in Cystic Fibrosis Patients With G542X Allele**
  - **Dosing underway, on target for full enrollment 1Q**
    - **US Trial** NCT04135495
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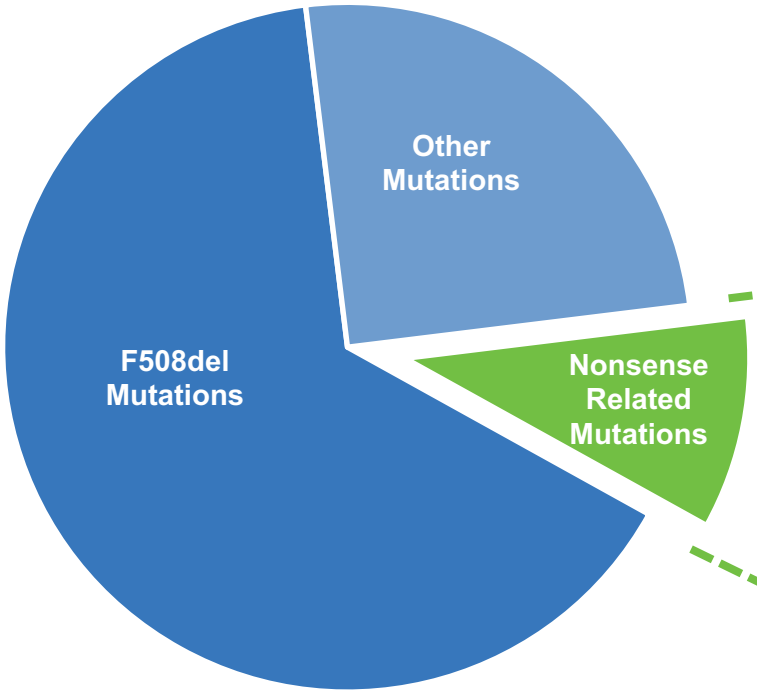
  - **Report on Topline Data in 1H 2020**
- **Phase 2 Protocol**
  - **Enrolling 8 patients with the G542X nonsense mutation on one or both alleles in the U.S; Enrolling up to 16 patients in EU/IL**
  - **Dosing patients in each trial; 4 increasing doses of ELX-02 ranging from 0.3 up to 3.0 mg/kg/day**
  - **Primary endpoints safety, tolerability and pharmacokinetics**
  - **Measuring changes in sweat chloride, FEV1 consistent with other Phase 2 trials for approved drugs**

Cystic Fibrosis Nonsense Mutation Patients Represent a Key Unmet Need Population

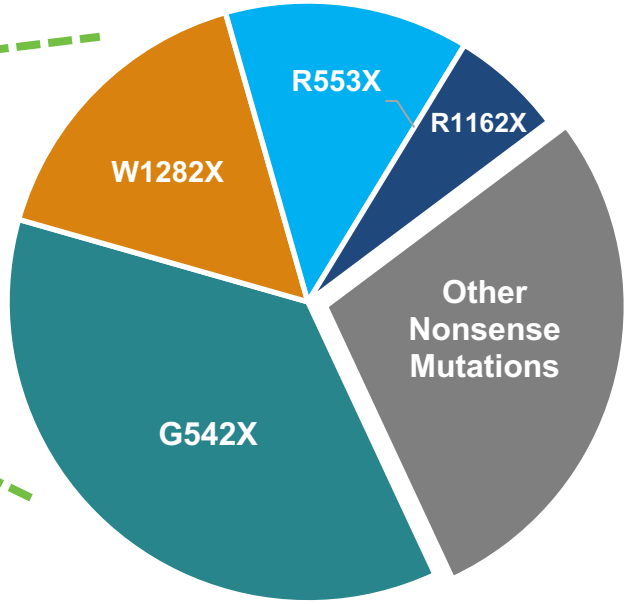
GLOBAL CYSTIC FIBROSIS PATIENTS
BY MUTATION/GENOTYPE



10 -13%

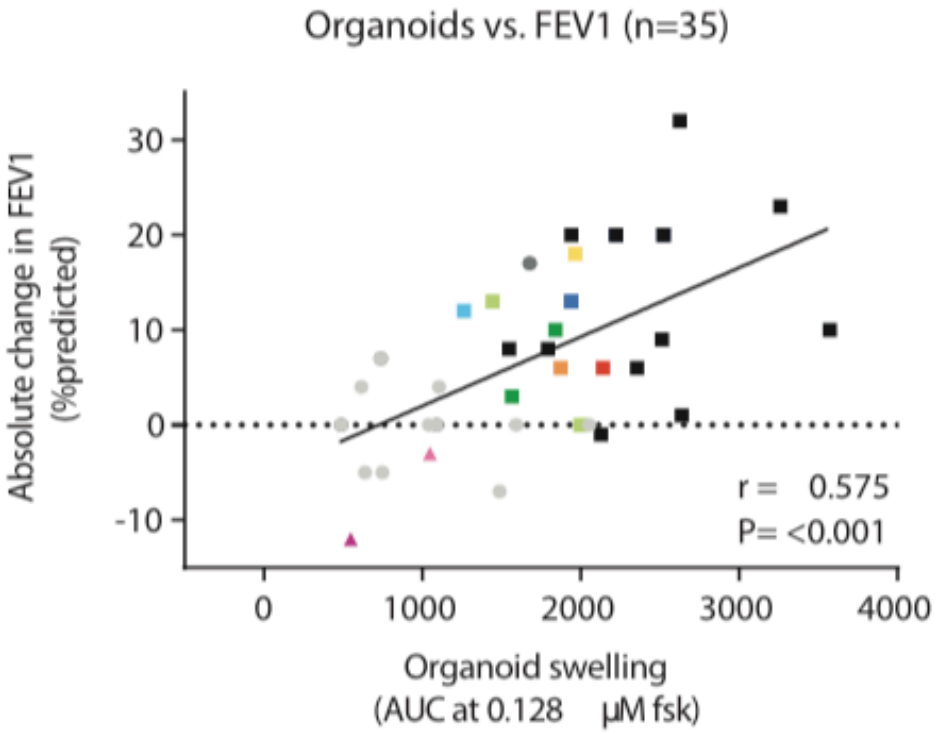
No Currently Approved Drugs
To Treat CFTR Nonsense Mutations

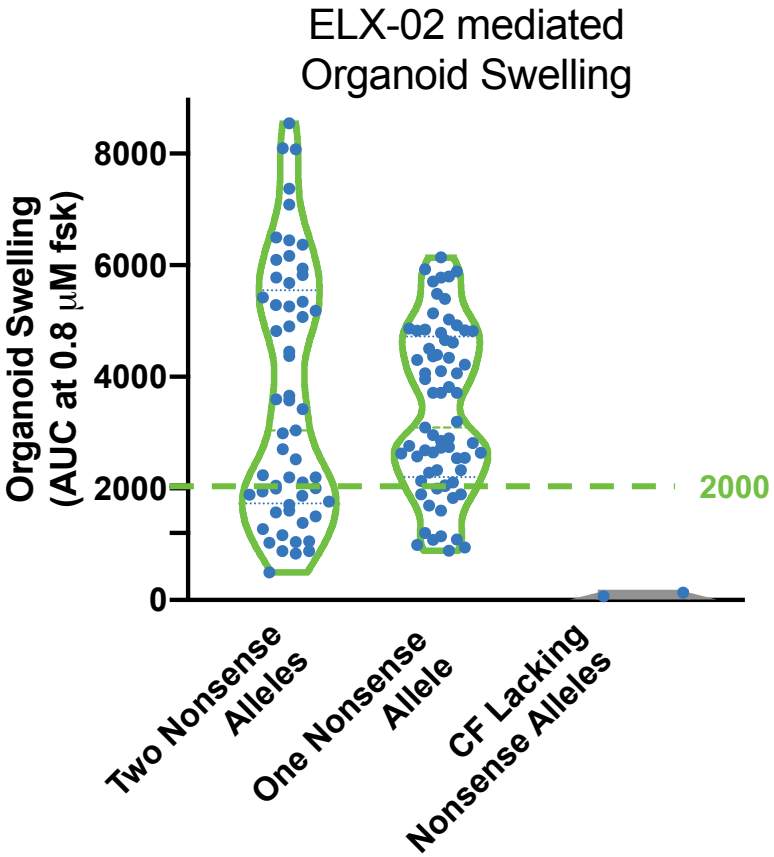
CFTR NONSENSE
MUTATION SUBTYPES



Source: Eloxx Internal Research/CFTR2 database

ELX-02 Response in Organoids Compares Favorably to Published Results



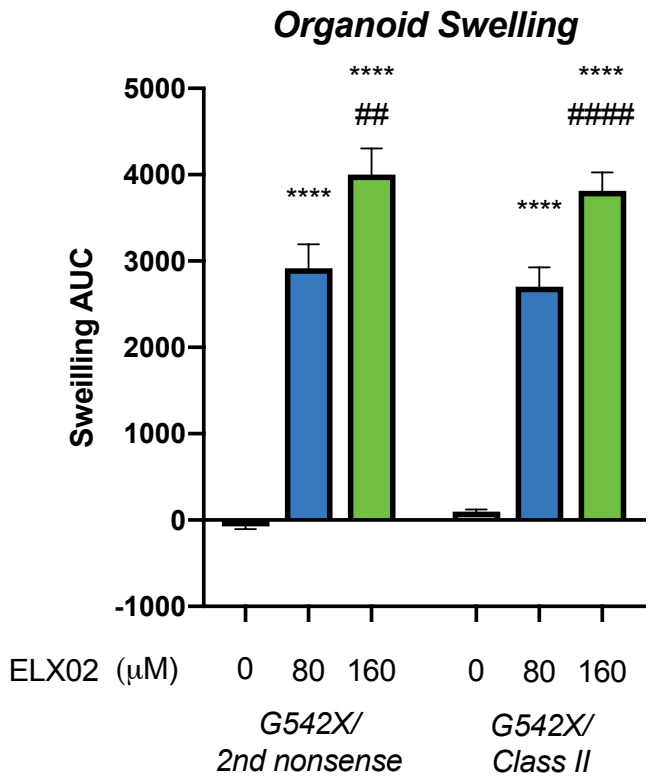


Berkers et al. Cell Reports (2019) Rectal Organoids Enable Personalized Treatment of Cystic Fibrosis.

Eloxx data on file.

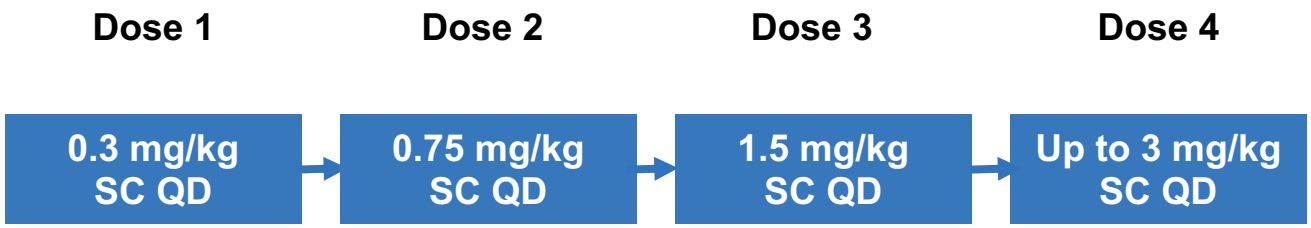
ELX-02 Mediated Organoid Swelling Is Equivalent in Organoids With One or Two Nonsense Mutations

- Significant increase in organoid swelling is observed in both G542X organoids with a second nonsense mutation and heterozygous organoids.
- Experiments used 0.8 µM Forskolin



ordinary one-way ANOVA with Tukey's multiple comparison testing was used,, **** p<0.0001 versus vehicle control, ## p<0.01 versus next lower concentration, , #### p<0.0001 versus next lower concentration. Data represent >40 biological replicates per group from 2 or 4 independent patient organoids, respectively.

Phase 2 Cystic Fibrosis – Trial Design



ClinicalTrials.gov Identifier: **US Trial** NCT04135495 **EU/IL Trial** NCT04126473

Population

- Up to 24 CF patients with a G542X mutation on one or both alleles (includes 8 patients in US)

Primary Outcome Measures

- Safety, tolerability, PK and pharmacodynamics of multiple doses of ELX-02

Secondary Outcome Measures

- Changes from baseline in sweat chloride levels and FEV1 following ELX-02

Locations

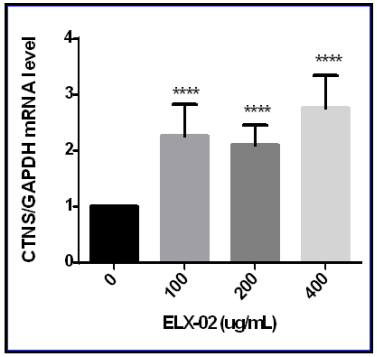
- USA, Israel, Germany, Belgium

ELX-02: Phase 2 Cystinosis Top Line 1st Cohort Results

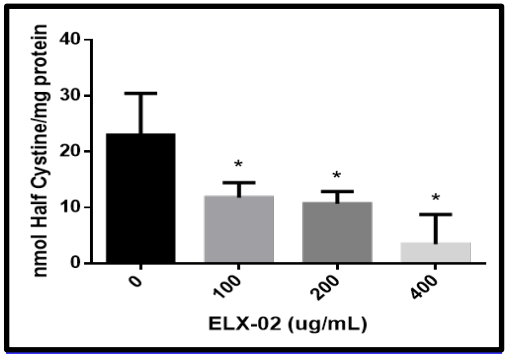
- **Overview**
  - ✓ 3 homozygous W138X male and female patients ages 23 to 38, with prior kidney transplants and varying degrees of renal insufficiency
  - ✓ Exposure achieved with dose adjustment based on individual eGFR
  - ✓ Three increasing doses of ELX-02 ranging from 0.3 up to 2.0 mg/kg/day
- **Phase 2 Cystinosis Results from 1st Cohort**
  - ✓ These promising reductions in WBC cystine provide a clear indication of ELX-02 biologic activity at nominal doses > 0.5mg/kg/day.
  - ✓ Safety Review Committee has approved progressing to the second cohort with targeted enrollment of 3 additional patients ages 12 and older.
  - ✓ Non-dilutive funding from Genome Quebec and Genome Canada
  - ✓ Cystinosis Research Foundation provided funding for preclinical phase

ELX-02: Supportive Preclinical Nephropathic Cystinosis Data

in vitro model
CTNS$^{W138X/W138X}$
fibroblasts

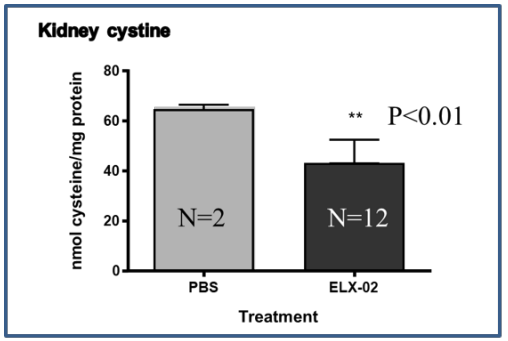


Nonsense-mediated mRNA decay



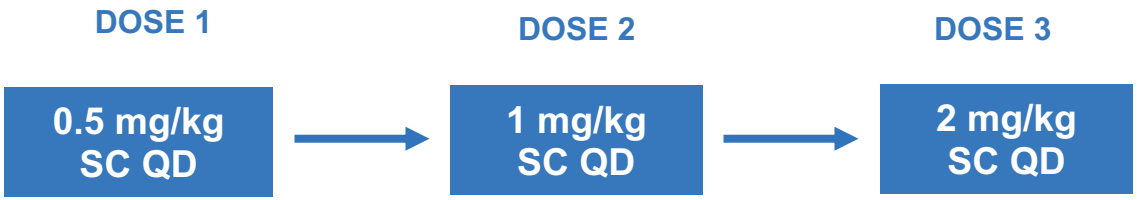
Cystine Accumulation

CTNS$^{Y226X/Y226X}$ knock-in



Cystine Accumulation

Nephropathic Cystinosis Study Design (EL-003)



ClinicalTrials.gov Identifier: NCT04069260

Population

- Nephropathic cystinosis participants with biallelic CTNS mutations, including at least one nonsense mutation

Primary outcome measures

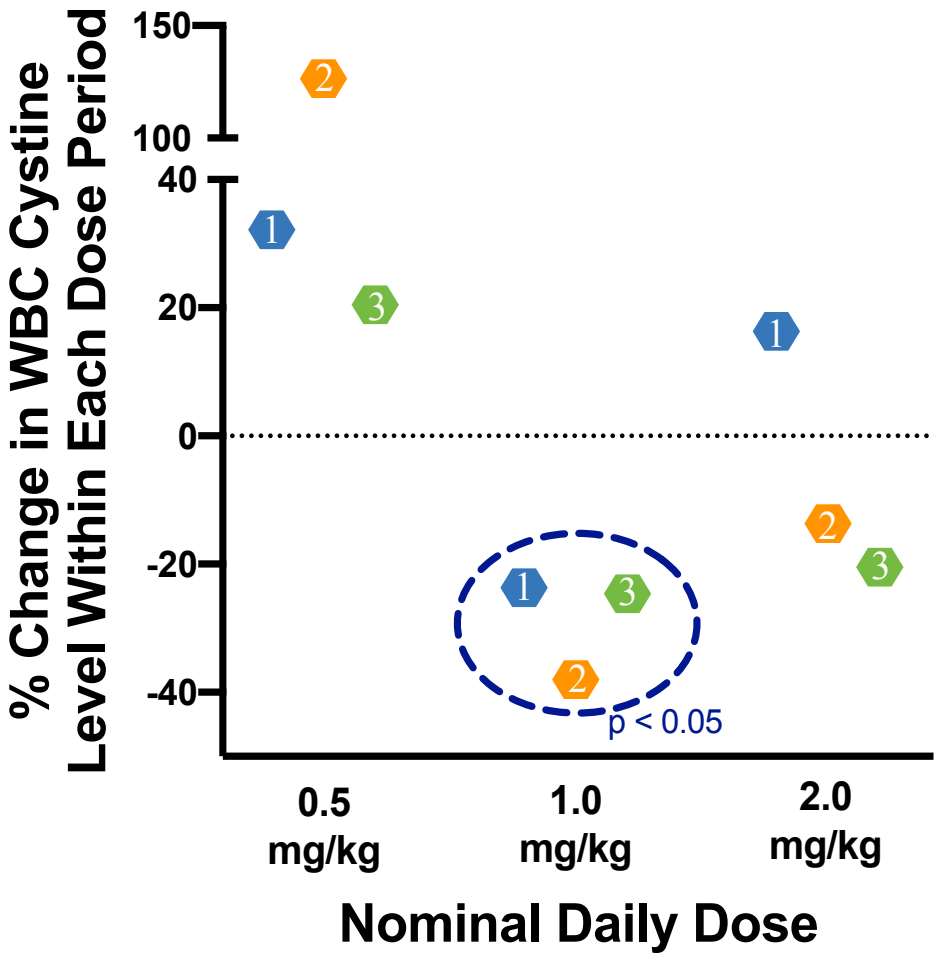
- Safety, tolerability, PK and pharmacodynamics of multiple doses of ELX-02

Secondary outcome measures

- Changes from baseline in white blood cell cystine levels following ELX-02

ELX-02 Demonstrates Biological Activity

Statistically Significant Reductions in WBC Cystine



- Change in White Blood Cell Cystine from baseline (pre-dose to last dose)
- The 1.0mg/kg nominal dose group demonstrated significant reduction in WBC; 2/3 patients in 2.0mg/kg nominal dose group showed reduction in WBC
- In the drug free interval between doses the patients experienced an increase in baseline WBC
- Results demonstrate biological activity for ELX-02 at nominal doses >0.5 mg/kg daily SubQ

Cystinosis Phase 2 Results – 1st Cohort

Pharmacokinetics, Safety, Tolerability

- ✓ **ELX-02 demonstrated pharmacokinetics consistent with previous studies and successfully achieved targeted nominal dose exposure based on adjustment for individual patient renal function.**
- ✓ **ELX-02 was generally well tolerated, with no deaths, nephrotoxicity, ototoxicity or serious adverse events. During the study, mild injection site reactions were reported.**
- ✓ **Importantly, there were no meaningful changes in eGFR or creatinine consistent with preservation of kidney function in these post- transplant patients.**

Patient	Lab Test	Screening	DG1 Pre-dose		DG2 Pre-dose		DG3 Pre-dose			4-Week Safety Follow Up
			Day 1	Day 7	Day 1	Day 7	Day 1	Day 7	Day 14	
1	Serum Creatinine µmol/L	132	117	126	128	138†	128	120	116	136
2		180	126	110	122	113	128	115	129	130
3		167	145	124	129	131	146	143	140	150
1	eGFR mL/min/ 1.73m²	44	51	47	46	42†	46	49	52	43
2		45	69	81	72	79	68	77	67	66
3		49	58	70	67	66	58	59	61	56

† Day 5 value

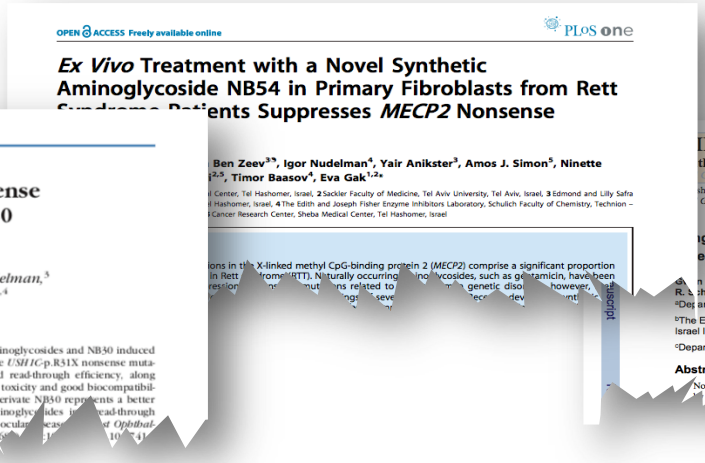
Cystinosis Next Steps

- Results demonstrate biological activity for ELX-02 at nominal doses >0.5 mg/kg daily SubQ represents human proof of concept and de-risks applications of this dosing range

- Safety Review Committee has approved progressing to the second cohort with targeted enrollment of 3 additional patients ages 12 and older.

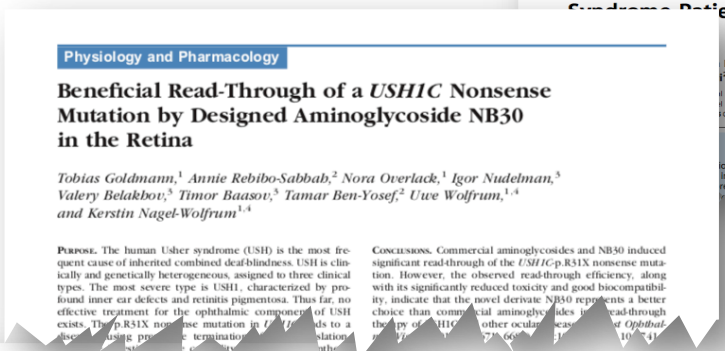
- Eloxx is reviewing the data with a panel of cystinosis scientific and clinical experts to determine if protocol modifications would be appropriate before initiating cohort 2 of this study.

Eloxx is Developing New Indications for its ERSG Library to Expand the Portfolio

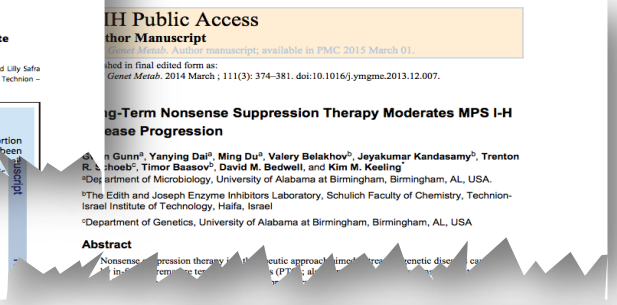

OPEN ACCESS Freely available online

PLoS one

***Ex Vivo* Treatment with a Novel Synthetic Aminoglycoside NB54 in Primary Fibroblasts from Rett Syndrome Patients Suppresses *MECP2* Nonsense**


Physiology and Pharmacology

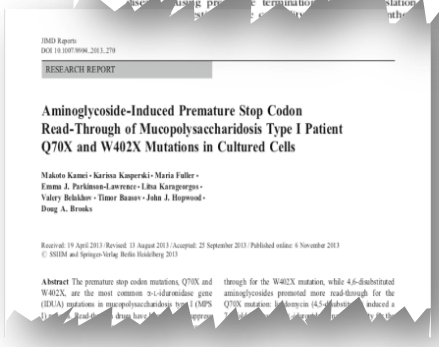
Beneficial Read-Through of a *USH1C* Nonsense Mutation by Designed Aminoglycoside NB30 in the Retina


NIH Public Access

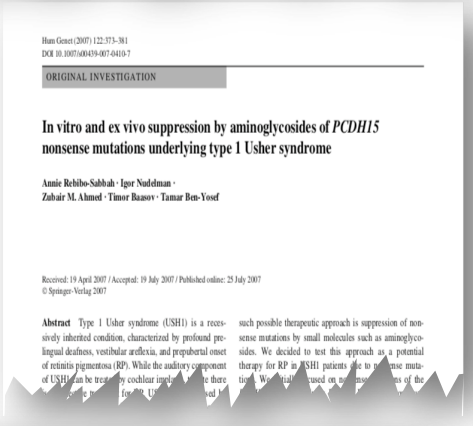
Author Manuscript

Genet Metab. Author manuscript; available in PMC 2015 March 01.

Long-Term Nonsense Suppression Therapy Moderates MPS I-H Disease Progression

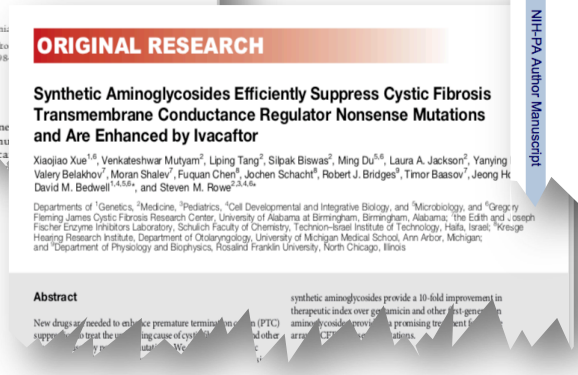

RESEARCH REPORT

Aminoglycoside-Induced Premature Stop Codon Read-Through of Mucopolysaccharidosis Type I Patient Q70X and W402X Mutations in Cultured Cells

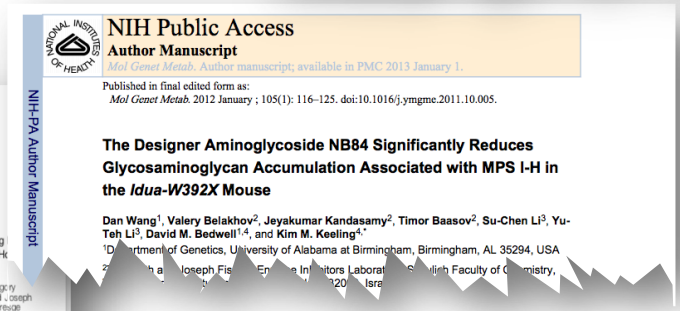

ORIGINAL INVESTIGATION

In vitro and ex vivo suppression by aminoglycosides of *PCDH15* nonsense mutations underlying type 1 Usher syndrome


Aminoglycoside antibiotics restore dystrophin function to skeletal muscles of *mdx* mice


ORIGINAL RESEARCH

Synthetic Aminoglycosides Efficiently Suppress Cystic Fibrosis Transmembrane Conductance Regulator Nonsense Mutations and Are Enhanced by Ivacaftor


NIH Public Access

Author Manuscript

Mol Genet Metab. Author manuscript; available in PMC 2013 January 1.

The Designer Aminoglycoside NB84 Significantly Reduces Glycosaminoglycan Accumulation Associated with MPS I-H in the *Idua-W392X* Mouse

ADPKD Overview

- 200,000-600,000 people with ADPKD in the US
  - 12 million people worldwide
- ~141,000 diagnosed cases of ADPKD in the US

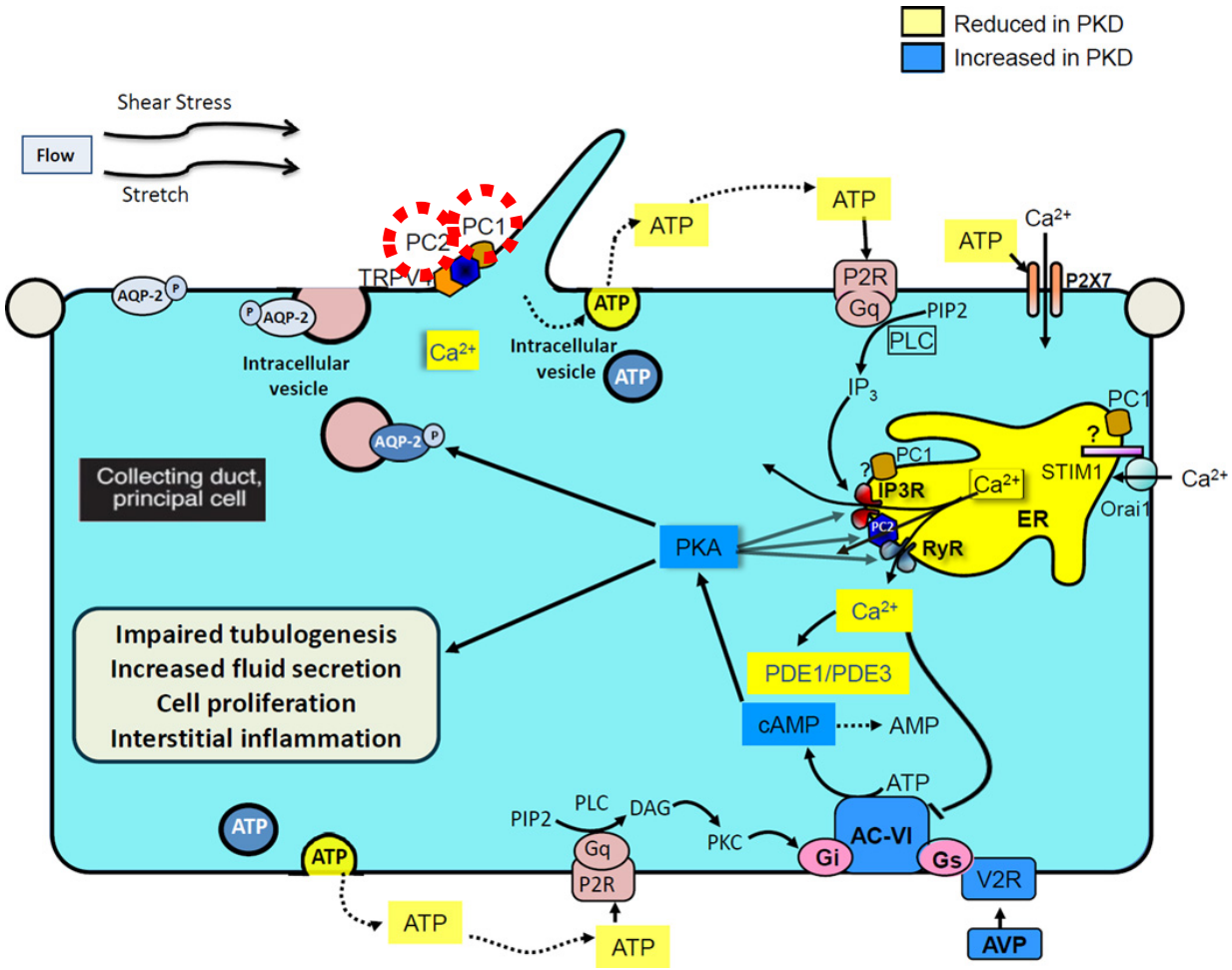
PKD1 Mutation
- 85% of all ADPKD cases
- Cysts may appear when patients are young adults
- Disease can progress rapidly
- Median age of ESRD onset is 54 yrs
- Gene location: short arm on chromosome 16 (16p13.3)

PKD2 Mutation
- 15% of all ADPKD cases
- Disease progresses more slowly vs. PKD1
- Median age of ESRD onset is 74 years
- Gene location: long arm on chromosome 4 (4q21)

- ~6,000 new cases diagnosed each year in the US
- ***~6-10% of individuals receiving dialysis and renal transplant treatment in the US have ADPKD***

1 Blanchette, C. et al; Burden of Autosomal Dominant Polycystic Kidney Disease: Systematic Literature Review, Am J Pharm Benefits, 2015; 7(2): e27-e36
2 Uncoverpkd.com (Otsuka HCP site)
3 NORD, https://rarediseases.org/rare-diseases/autosomal-dominant-polycystic-kidney-disease/
4 PKD International, https://pkdinternational.org/what-is-pkd/adpkd

Targeting PC1 and PC2 Protein Restoration



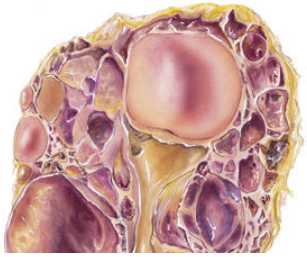
"PC1 is a low abundance protein in humans, who appear to be highly sensitive to reductions in its expression"

Source: Organoid cystogenesis reveals a critical role of microenvironment in human polycystic kidney disease; Curz et al Nat Mater. 2017 November

ADPKD Overview *(Autosomal dominant polycystic disease)*

- Genetic disorder characterized by cysts localized within the kidney. Majority of patients progress to ESRD.
- Mutations in PKD1 or PKD2 cause a disruption in the production of polycystin, which through multiple signaling process leads to excess vasopressin, leading to cyst growth.

ADPKD: Cyst formation



ADPKD US:
140k diagnosed pts.

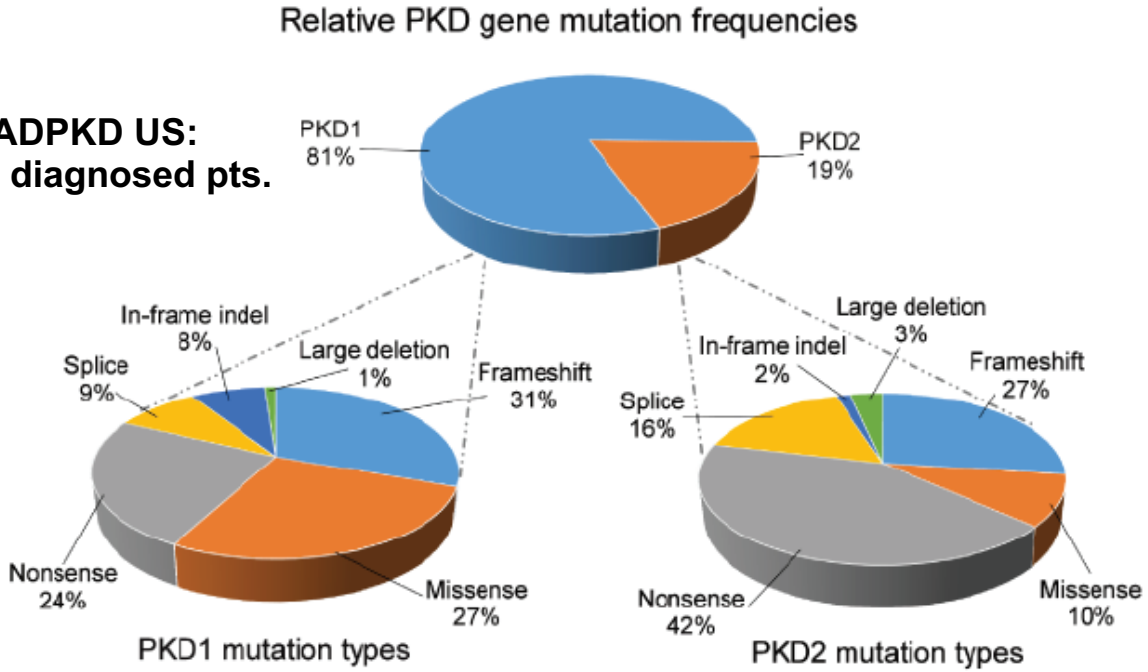
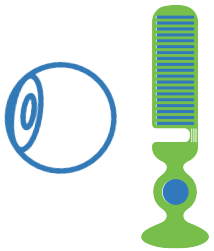


Figure 2. Frequency and type of *PKD1* and *PKD2* mutations from the PKD mutation database. All mutation types have been reported for both genes. The relative infrequency of missense mutations and in-frame insertions or deletions for *PKD2* could reflect the under-diagnosis of these patients present in the general population. The PKD mutation database is available at http://pkdb.mayo.edu/index.html (accessed 22 April 2016).

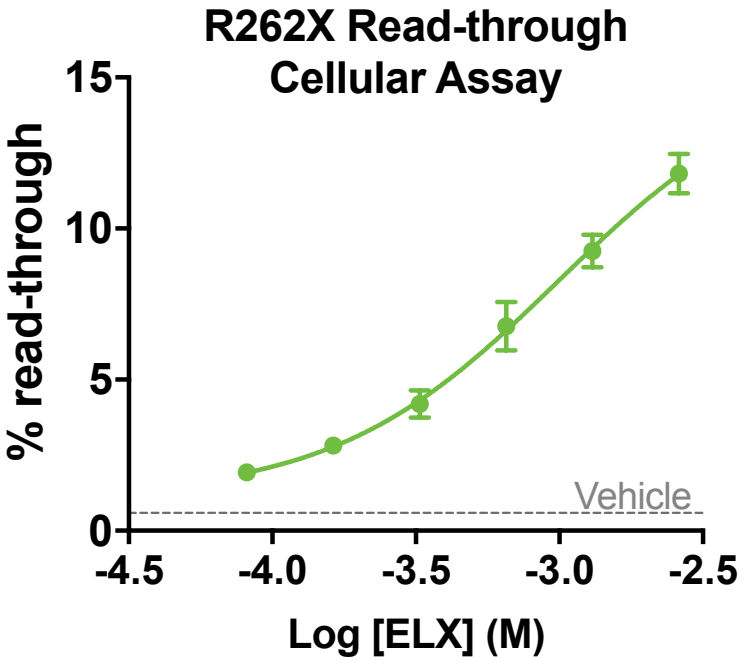
Ocular Program Development



- High unmet medical need and prevalence of nonsense mutations across inherited retinal diseases (IRDs)
- Screened multiple compounds from ERSG library for read-through and tolerability
- IND-enabling studies are progressing
- Emerging Profile Across Models
  - Compounds are appropriate for intravitreal administration
  - Compounds show retinal tolerability at doses 10-fold greater than anticipated efficacy range in sensitive species
    - No adverse ELX compound-related retinal anatomic or functional changes observed to date by histopathology and ERG
  - Dose-dependent read-through of Usher mutations greater than gentamicin reference
  - Encouraging PK demonstrating retina exposure
- Growing team of ophthalmic expertise
- Support from the FFB and Research Community

In Vivo Modeling for Intravitreal Administration Evaluation

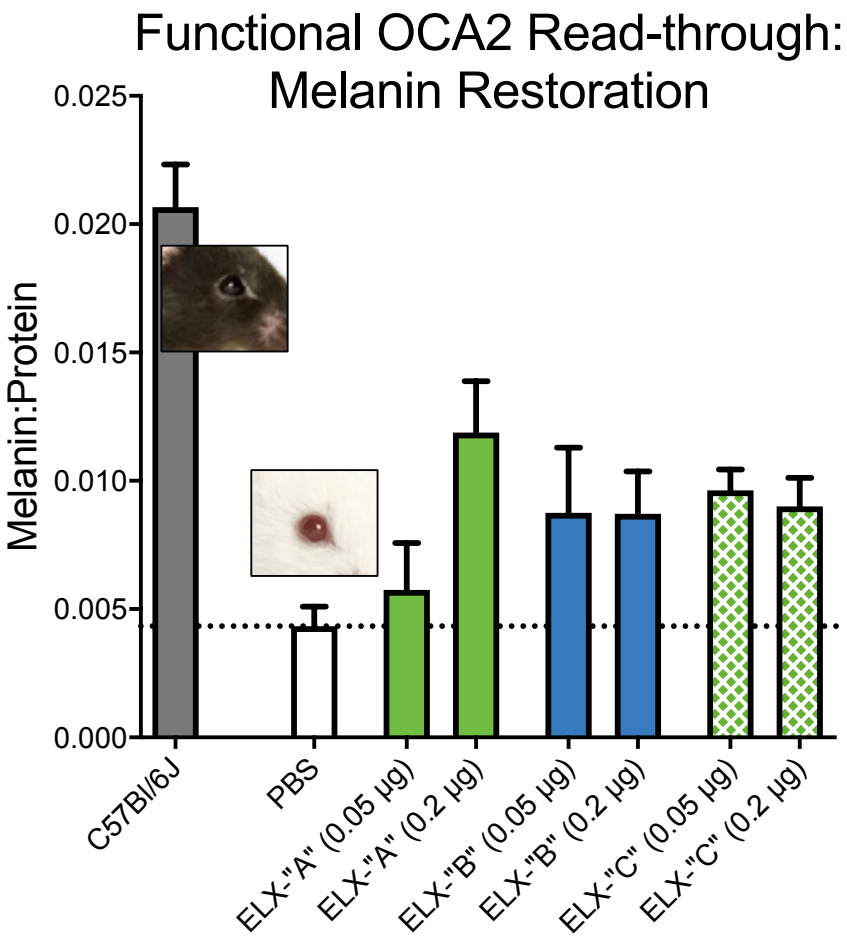
- SJL/J mice have a *R262X* mutation (UGA) in the *Oca2* gene[1]
- OCA2 is a channel involved in establishing organelle (melanocyte) pH in the RPE[2]
- Cellular read-through testing demonstrates significant read-through potential across ELX compounds
- Model is being used to screen Eloxx compounds for *in vivo* read-through activity at the back of the eye



1. Shoji et al, Exp. Anim 2015; 64(2)
2. Bellono et al., eLife 2014

ERSGs Promote Functional Read-through in the Eye by Intravitreal Administration

- Intravitreal dosing of ELX compounds demonstrate a dose-dependent increase in melanin production in the eye
  - Single dose on Study Day 1
  - Melanin measured on Study Day 3
- Multiple ERSG compounds demonstrate increased OCA2 function after single intravitreal injection
- Data support that ERSG compounds can reach cells deep in the neurosensory retina, including the retinal pigment epithelium and choroid
- New data to be presented at the **Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting** May 3-5, 2020 Baltimore, MD



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Thank you.

Investor Presentation
January 2020