Eloxx Pharmaceuticals

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

2019 Cantor Global Healthcare Conference
October 3, 2019

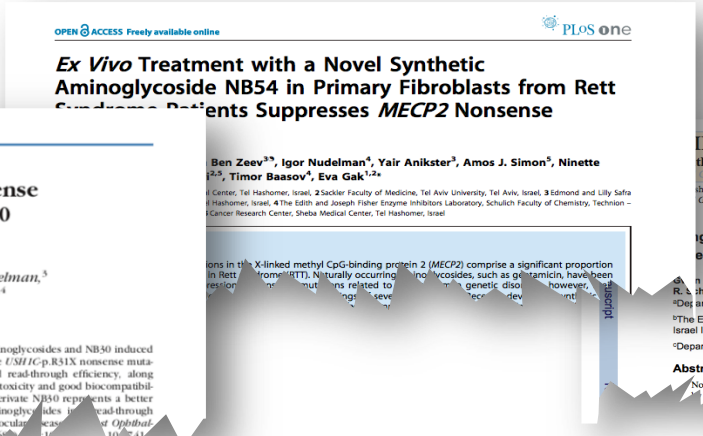
Forward-Looking Statements

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

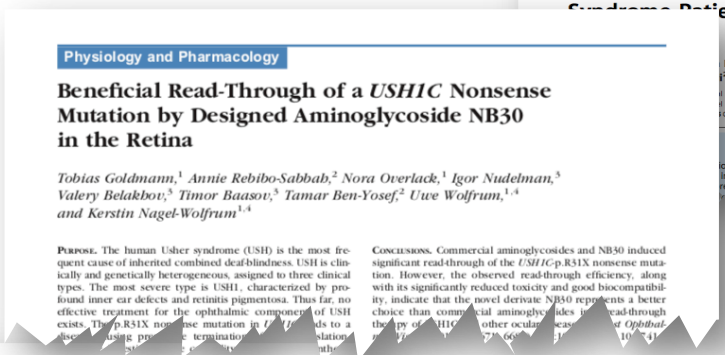
- **Experienced Leadership Team**
- **Top Line ELX-02 Phase 2 Data in Cystic Fibrosis and Cystinosis in 2019**
  - **Phase 2 ELX-02 Clinical Trial in Cystic Fibrosis**
    - **Cystic Fibrosis Foundation Provided Funding & Additional Support, Protocol Sanctioned by the Cystic Fibrosis Therapeutics Development Network**
    - **Dr. Ahmet Uluer, Director of Adult Cystic Fibrosis Program, Boston Children's Hospital, U.S. Lead Investigator**
    - **Dr. Eitan Kerem, Head of Division of Pediatrics, Children's Hospital, Hadassah Medical Center, Global Lead Investigator**
  - **Phase 2 ELX-02 Clinical Trial in Cystinosis**
    - **Non-dilutive funding from Genome Quebec and Genome Canada**
    - **Dr. Paul Goodyer, Professor of Pediatrics, McGill University, Principal Investigator**
- **New Indication Screening Ongoing (Eye, Kidney, Lung)**
- **Actively Developing Business Development Opportunities to Advance Full Pipeline and Expand Therapeutic Programs**

Novel ESRG Library has Demonstrated Activity across Multiple Orphan Diseases

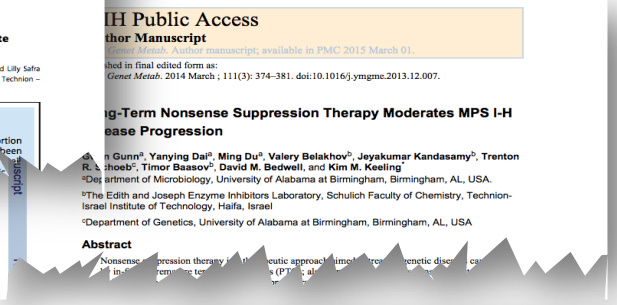

OPEN ACCESS Freely available online

PLoS one

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


Physiology and Pharmacology

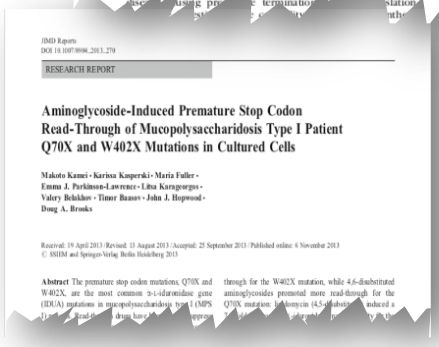
Beneficial Read-Through of a *USH1C* Nonsense Mutation by Designed Aminoglycoside NB30 in the Retina


NIH Public Access

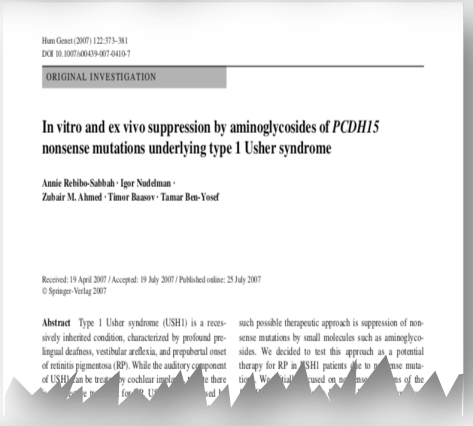
Author Manuscript

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

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

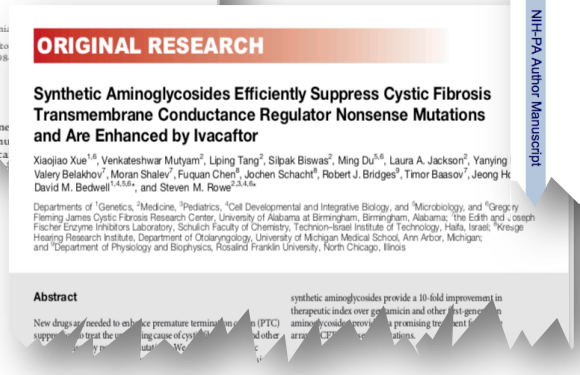

RESEARCH REPORT

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

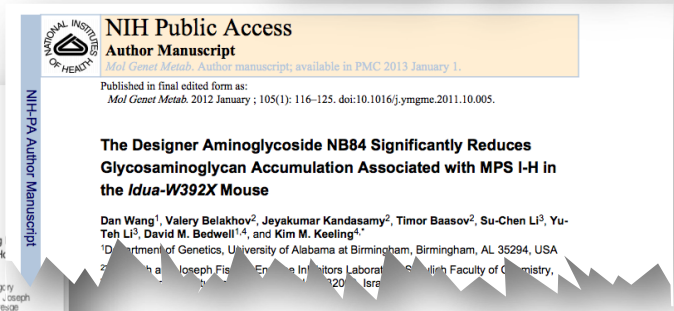

ORIGINAL INVESTIGATION

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

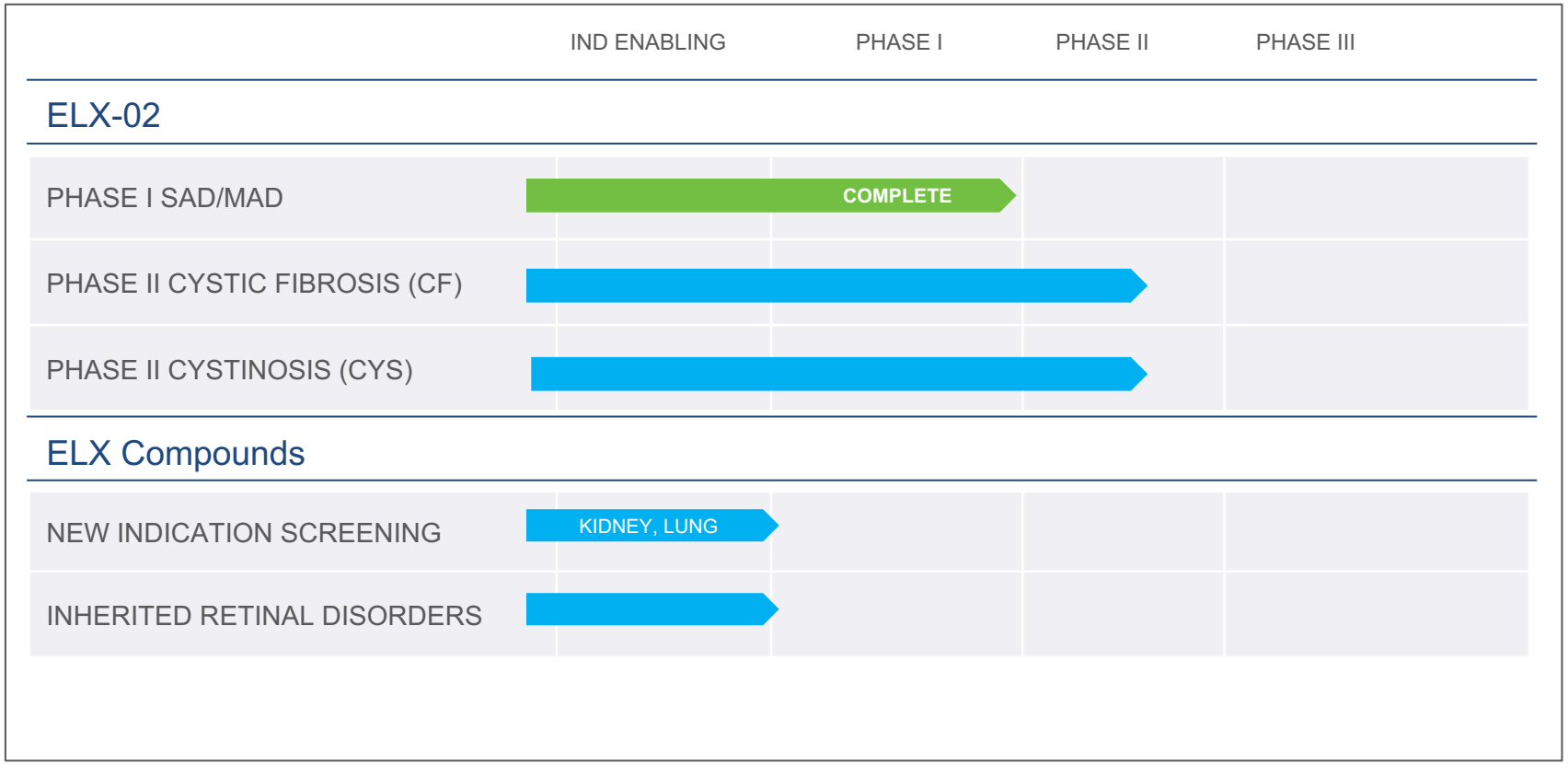

NIH Public Access

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

Eloxx Pipeline
Phase 2 Top Line Data This Year in CF 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 ECSF 2019
- ○ **Full data presentations at NACFC Oct. 31- Nov. 2, 2019**

MAD
(multiple ascending dose)

- ○ **Full data presentations at NACFC Oct/Nov 2019**
- ○ **CSR and manuscript to follow**

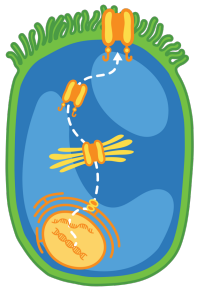
Renal Impairment

- ○ **Full data presentations at 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)

ELX-02: Preclinical Data De-Risks Phase 2

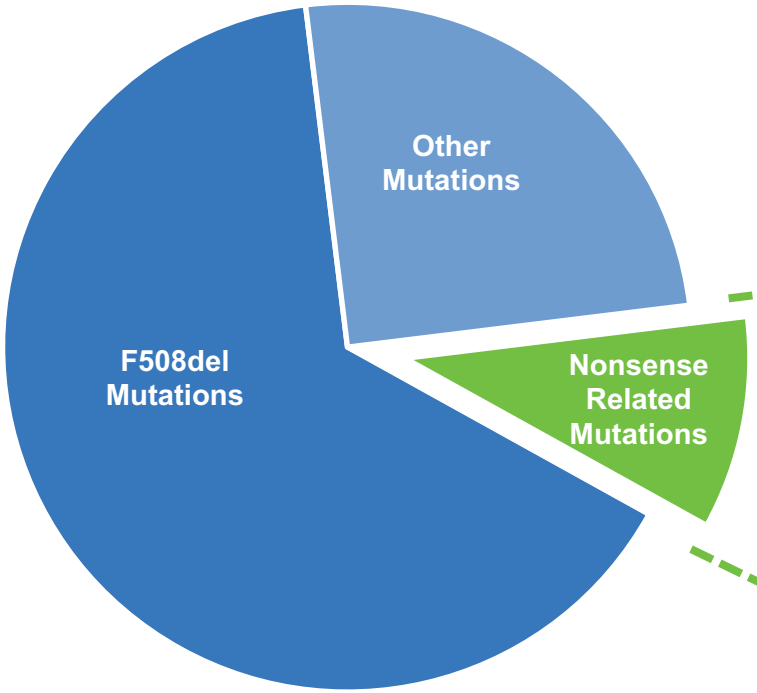


- ELX-02 is a small molecule that permits read-through of nonsense mutations
  - ✓ High selectivity for the eukaryotic cytoplasmic ribosome relative to mitochondrial ribosome
  - ✓ Defined MOA: Demonstrated significant increases in Cystinosin & CFTR *mRNA*, protein and function
  - ✓ Demonstrated read-through 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

Our Orphan Drug Programs Have Strong Advocacy Support

Cystic Fibrosis Nonsense Mutation Patients Represent a Key Unmet Need Population

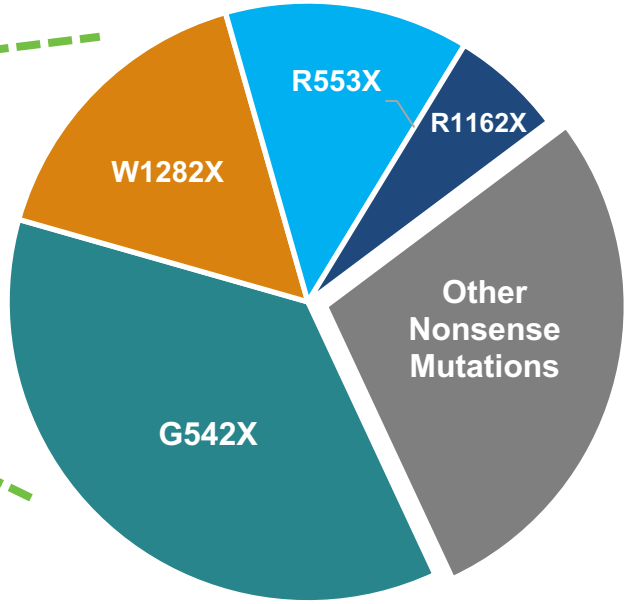
GLOBAL CYSTIC FIBROSIS PATIENTS
BY MUTATION/GENOTYPE



10 -13%

No Currently Approved Drugs
To Treat CFTR Nonsense Mutations

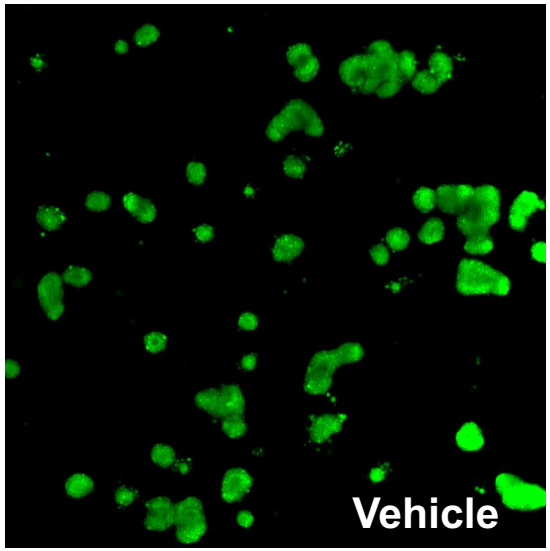
CFTR NONSENSE
MUTATION SUBTYPES



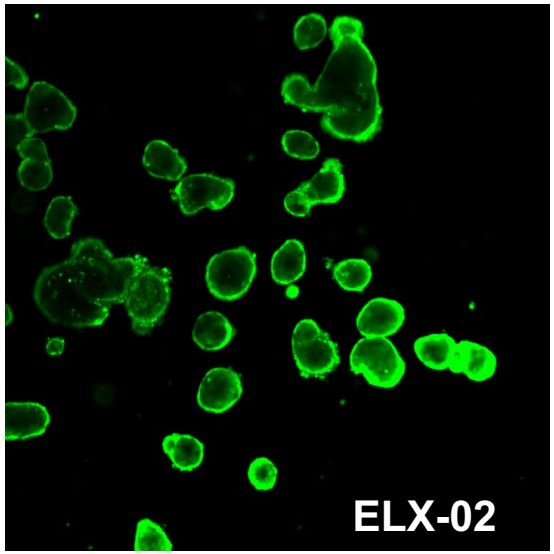
Source: Eloxx Internal Research/CFTR2 database

Organoid Swelling Assay Demonstrates CFTR Function

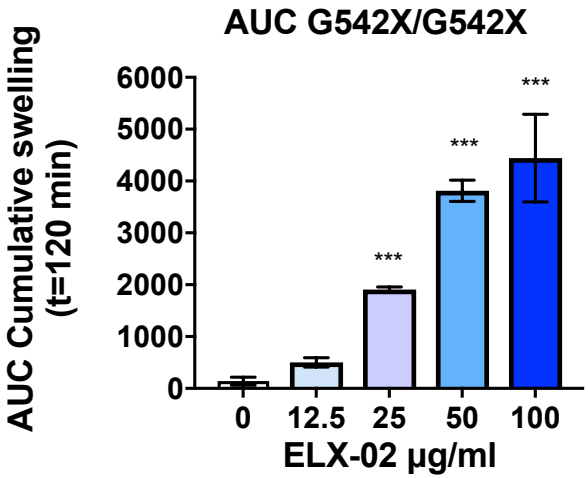
Cystic Fibrosis Organoid dose-responsive swelling assay response



Patient Organoid without drug treatment: No Swelling of Organoids

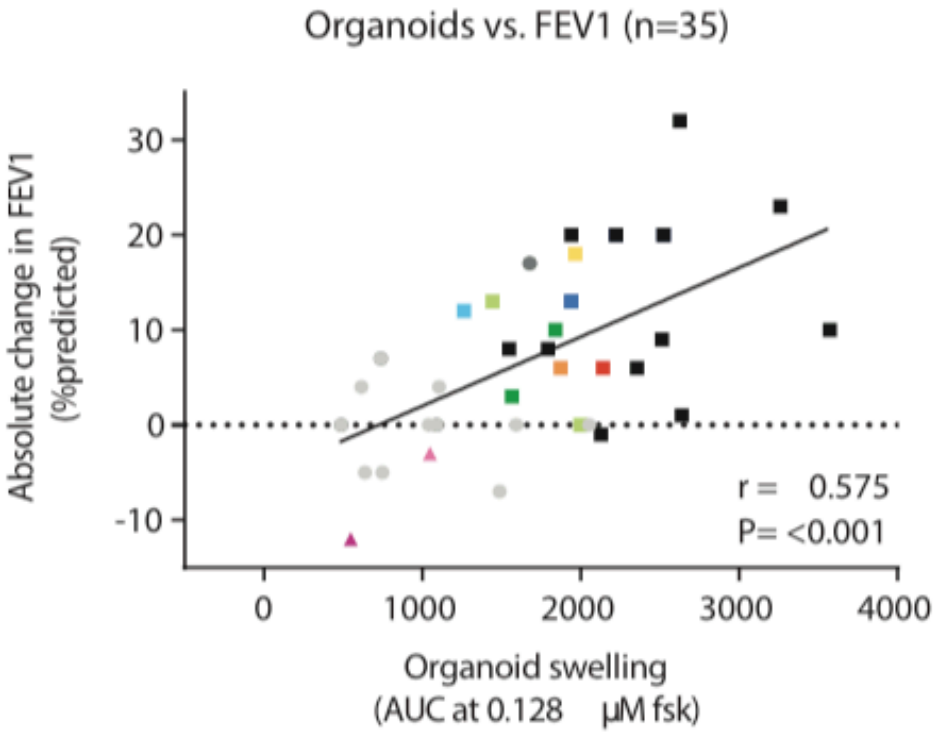


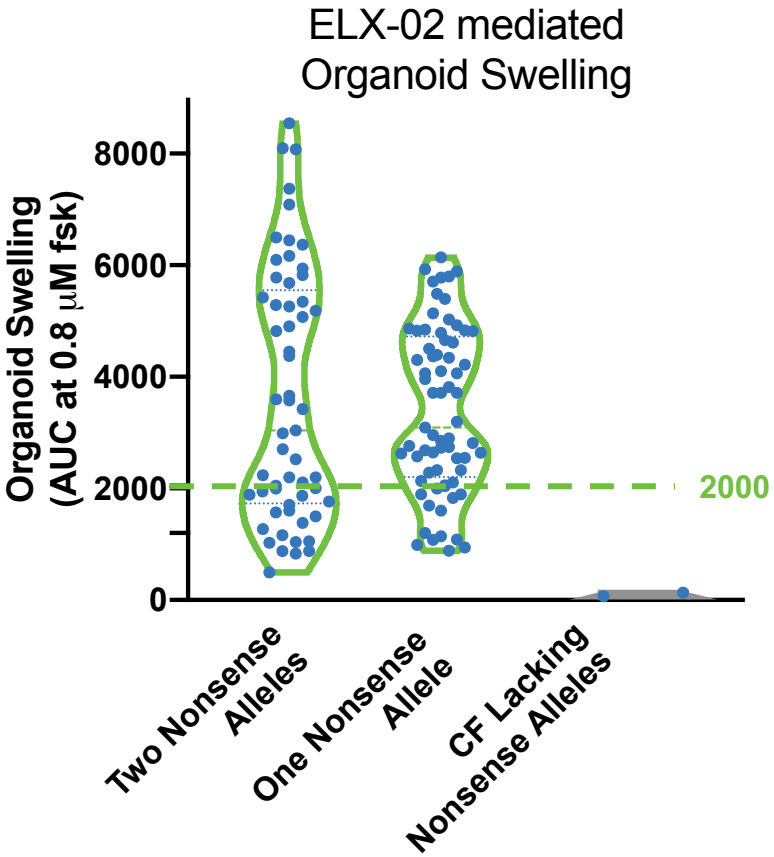
Patient Organoid with ELX-02 treatment: Swelling of Organoids



Swelling quantification of patient organoid with ELX-02 treatment.

ELX-02 Response in Organoids Compares Favorably to Published Results



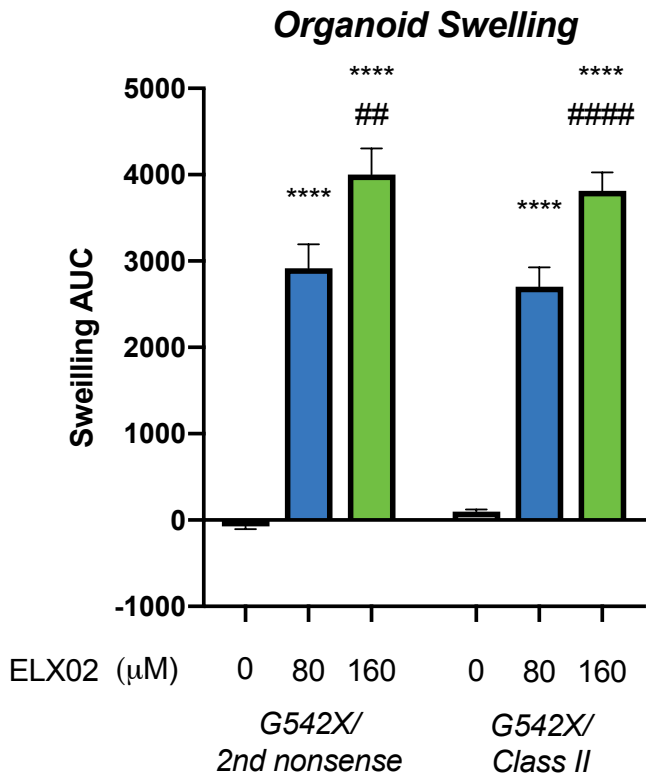


Berkers et al. Cell Reports (2019) Rectal Organoids Enable Personalized Treatment of Cystic Fibrosis.

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

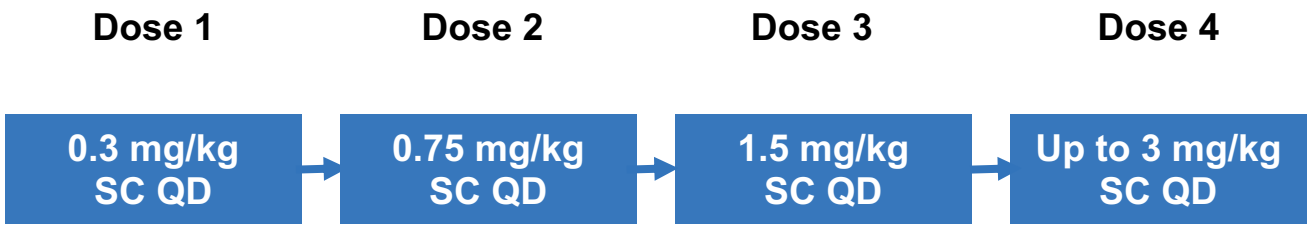


ordinary one-way ANOVA with Tukey's multiple comparison testing was used,, **** p<0.0001 versus vehicle control, ## p<0.01 versus next lower concentration, , #### p<0.0001 versus next lower concentration. Data represent >40 biological replicates per group from 2 or 4 independent patient organoids, respectively.

ELX-02: Phase 2 CF Top Line in 2019

- **Phase 2 Clinical Trial Program**
  - ✓ Cystic Fibrosis Foundation Provided Funding, Protocol Sanctioned by the Cystic Fibrosis Therapeutics Development Network
  - ✓ Clinical Trial Application (CTA) approved, EU CFS “high priority” for Phase 2 Protocol
  - ✓ Dr. Ahmet Uluer, Director, Adult Cystic Fibrosis Program at Boston Children’s Hospital, US Lead Investigator
  - ✓ Dr. Eitan Kerem, Head of Division of Pediatrics, Children’s Hospital, Hadassah Medical Center, Global Lead Investigator
- **Phase 2 Protocol**
  - Enrolling up to 24 patients with the G542X nonsense mutation on one or both alleles in the U.S., Europe and Israel
  - 4 increasing doses of ELX-02 ranging from 0.3 up to 3.0 mg/kg/day
  - Measuring changes in sweat chloride consistent with other Phase 2 trials for approved drugs

Phase 2 Cystic Fibrosis – Trial Design



Population

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

North American Cystic Fibrosis Conference (NACFC) October 31 - November 2, 2019

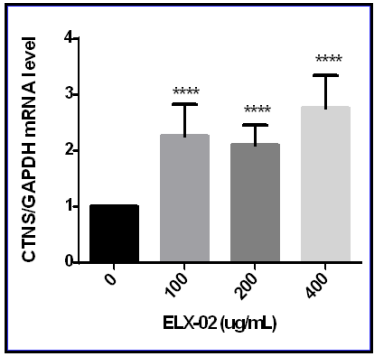
"Investigational Drug ELX-02 Mediates CFTR Nonsense Mutation Read-through To Increase *CFTR m*RNA CFTR Protein Translation and CFTR Function"
November 1, 2019 2:15 p.m. -3:50 p.m. CDT ORAL Workshop: New & Emerging Therapies to Correct the Basic Defect"

"Pharmacokinetics, Safety, and Tolerability of Multiple Ascending Doses of ELX-02 in Healthy Volunteers, a Potential Treatment for Cystic Fibrosis Caused by Nonsense Mutations" **October 31, 2019 11:15 a.m. – 1:45 p.m. CDT POSTER Session 1**

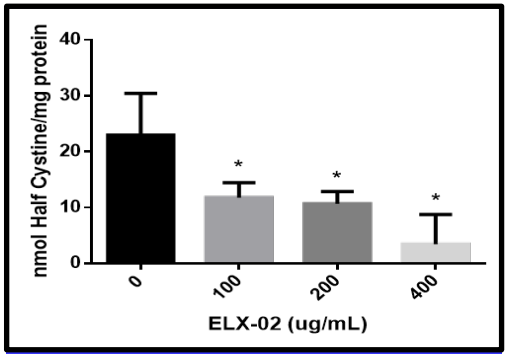
"Pharmacokinetics, Safety, and Tolerability of Single Ascending Doses of ELX-02 in Healthy Volunteers, a Potential Treatment for Cystic Fibrosis Caused by Nonsense Mutations" **October 31, 2019 !!:15 a.m. – 1:45 p.m. CDT POSTER Session 1**

ELX-02: Supportive Preclinical Nephropathic Cystinosis Data

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

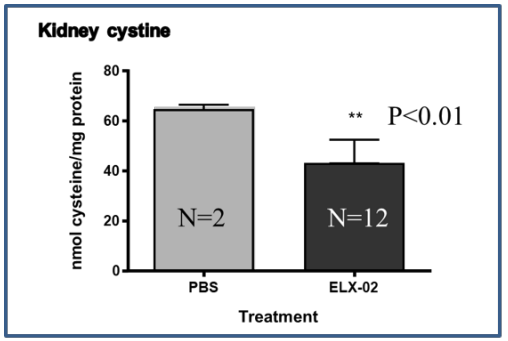


Nonsense-mediated mRNA decay



Cystine Accumulation

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

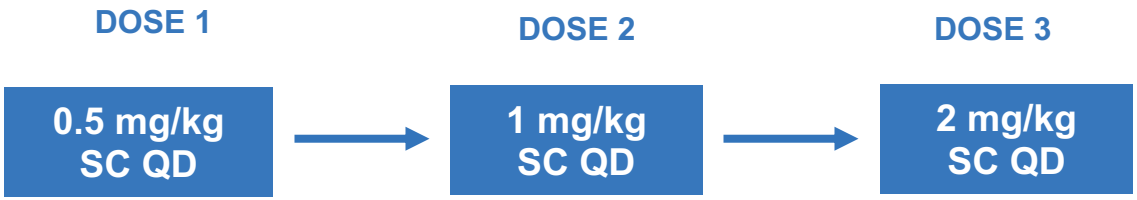


Cystine Accumulation

ELX-02: Phase 2 Cystinosis Top Line in 2019

- **Phase 2 Clinical Trial Program**
  - ✓ Enrolling in Canada
  - ✓ Non-dilutive funding from Genome Quebec and Genome Canada
  - ✓ Cystinosis Research Foundation provided funding for preclinical phase
  - ✓ Dr. Paul Goodyer, Professor of Pediatrics at McGill University is the Principal Investigator
- **Phase 2 Protocol**
  - Enrolling up to 6 patients with nephropathic cystinosis with at least 1 nonsense mutation in the cystinosis gene
  - Three increasing doses of ELX-02 ranging from 0.3 up to 2.0 mg/kg/day
  - Measuring the dose-dependent effect of ELX-02 on cysteine levels in white blood cells

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

American Society of Nephrology (ASN) Kidney Week Conference Abstracts November 5-10, 2019

KIDNEYWEEK 2019
Washington, DC • Nov. 5 – 10

"An open label-single dose, parallel-group study to evaluate the effects of renal impairment on the pharmacokinetics of ELX-02: Results from subjects with mild and moderate renal impairment" - November 7, 2019 10:00 a.m. – 12:00 pm

"Cystinosis nonsense mutation read-through mediated by ELX-02 restores protein function using in vitro and in vivo models" - November 7, 2019 10:00 a.m. – 12:00 pm

Rare Kidney Diseases

- **> 150 identified Rare Kidney Diseases**
- **Overall Prevalence: 60-80 cases per 100,000**
- **Fifth most common cause of ESRD**

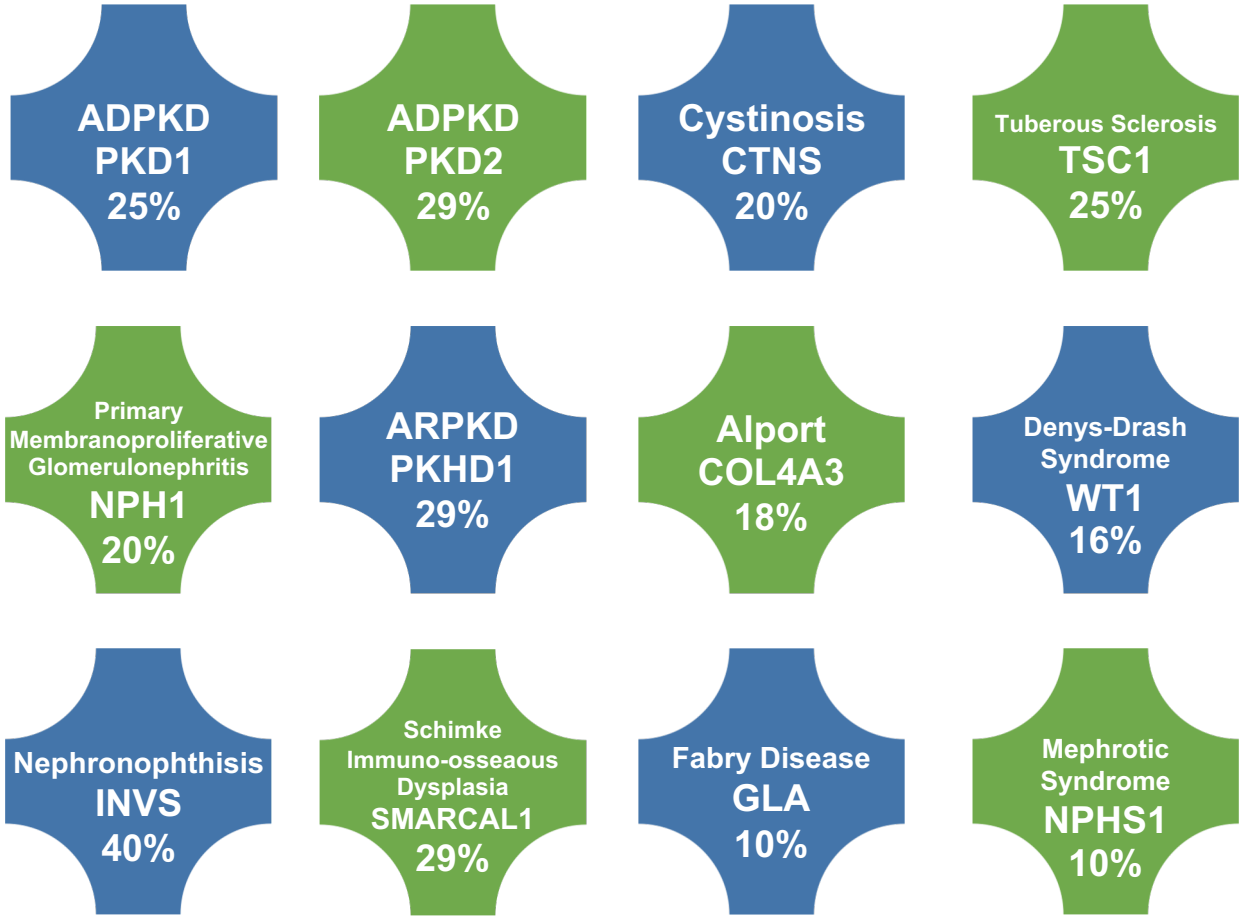
Patients with inherited kidney disorders rarely die
(many progress to renal transplantation)
Results in poor health, low quality of life, multisystemic complications.
Devuyst & Gauy-Woodford - KDIGO Conference (2016)

Nephropathic cystinosis is an autosomal recessive storage disease caused by defective transport of cystine out of lysosomes .The renal tubular damage of cystinosis, begins at 6 to 12 months of age, glomerular damage generally becomes apparent by 2 to 5 years of age and results in end-stage renal disease by 9 to 10 years of age unless cystine-depleting therapy is initiated early in life. Renal transplantation, often by age of 20, has transformed cystinosis from an exclusively pediatric disease to one that affects individuals up to (and potentially beyond) 50 years of age.

Nonsense mutations are an important genetic variation in a wide range of rare kidney disorders including: Nephropathic Cystinosis, Autosomal Dominant Polycystic Kidney Disease, Cystinuria, and others

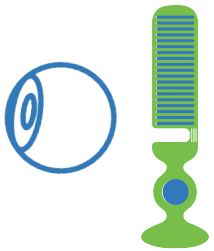
Nephrology NSM mediated disease opportunities

Inherited Disease
Target Gene
NSM %



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

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

Eloxx Pharmaceutical Highlights

- **Experienced Leadership Team**
- **Top Line ELX-02 Phase 2 Data in Cystic Fibrosis and Cystinosis in 2019**
  - **Phase 2 ELX-02 Clinical Trial in Cystic Fibrosis**
    - **Cystic Fibrosis Foundation Provided Funding & Additional Support, Protocol Sanctioned by the Cystic Fibrosis Therapeutics Development Network**
    - **Dr. Ahmet Uluer, Director of Adult Cystic Fibrosis Program, Boston Children's Hospital, U.S. Lead Investigator**
    - **Dr. Eitan Kerem, Head of Division of Pediatrics, Children's Hospital, Hadassah Medical Center, Global Lead Investigator**
  - **Phase 2 ELX-02 Clinical Trial in Cystinosis**
    - **Dr. Paul Goodyer, Professor of Pediatrics, McGill University, Principal Investigator**
    - **Non-dilutive funding from Genome Quebec and Genome Canada**
- **Reported Cash & Cash Equivalents at June 30, 2019 of $76.3M Funded through Top Line Data and into 2021**

Eloxx Pharmaceuticals

Thank you.

2019 Cantor Global Healthcare Conference
October 3, 2019