ELOXX
Eloxx Pharmaceuticals

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

38th Annual Cowen Healthcare Conference 2018

Forward-Looking Statements

Certain statements included in this presentation are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These include statements of management's intentions, belief, plans and future expectations and, therefore, you are cautioned not to place undue reliance on them. Such forward-looking statements involve risks and uncertainties and actual results could differ materially from any forward-looking statements expressed or implied herein.

The risks and uncertainties that could result in actual results to differ materially from those forward-looking statements expressed or implied herein include, but are not limited to: the Company's ability to continue as a going concern; the ability of the Company to consummate additional financings; the development of the Company's technology; the approval of the Company's patent applications; the Company's ability to successfully defend its intellectual property or obtain the 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 success of the Company's license agreements; the timing and success of the Company's preliminary studies, preclinical research, clinical trials and related regulatory filings; if approved, the acceptance by the market of the Company's products; and the continued quotation of the Company's common stock on the over-the-counter securities market, as well as other factors expressed from time to time in the Company's 10-K, 10-Qs and other filings with the SEC. The forward-looking statements contained herein are made only as of the date of this presentation, and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstances.

Eloxx Pharmaceuticals Highlights

Leading Read Through Company	**Clinical stage biopharmaceutical company** developing novel small molecule medicines designed to treat genetic diseases by restoring the production of proteins from genes with nonsense mutations
Experienced Management	**Management team with established track record** of successful product development and commercialization
Strong Clinical Focus	**On track for mid 2018 IND (FDA) and CTA (Belgium) submission** to support initiation of Phase 2 studies in Cystinosis and Cystic Fibrosis in 2018. Phase 1 SAD complete, MAD ongoing. Pediatric Orphan Opportunity.
Diversified Development Portfolio	**Global rights for library of novel molecules** that address the aminoglycoside/ribosome binding site. Anticipate advancing second compound to IND enabling studies in 2018.
Financially Sound	**Completed $38M Series C financing** at the end of 4Q 2017 **Extensive IP portfolio**; Composition of matter thru 2031 **Trading as ELOX ; March 20th Earnings Call for FY2017**

Highly Experienced US Leadership Team

Robert Ward
CHAIRMAN AND CEO

Radius · AstraZeneca

Pedro Huertas, MD, PhD
CMO

Pfizer · Shire

Gregory Weaver
CFO

Prometic · ORYZON

John van Duzer, PhD
VP CMC

Celgene · Acetylon Pharmaceuticals, Inc.

Barbara Ryan
INVESTOR RELATIONS

Radius · Deutsche Bank

Neil Sharpe, PhD
VP TRANSLATIONAL SCIENCE

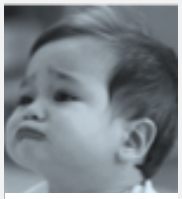
Biogen · MERCK

The Promise of Read-Through

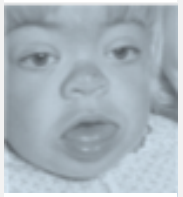
>1,800

Genetic diseases involve nonsense mutations

Cystic Fibrosis

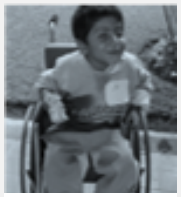


Cystinosis



MPS I Syndrome

Rett Syndrome



Duchenne Muscular Dystrophy

- In every genetic disease a subset of patients have nonsense mutations that impair the production of essential proteins
- Translational read through is directed at restoring the production of full length proteins by overcoming the premature stop codon and nonsense mediated decay

Aminoglycosides' tolerability profile historically limited suitability for read-through treatment of serious genetic diseases

Aminoglycosides first showed read-through activity in nonsense mediated diseases

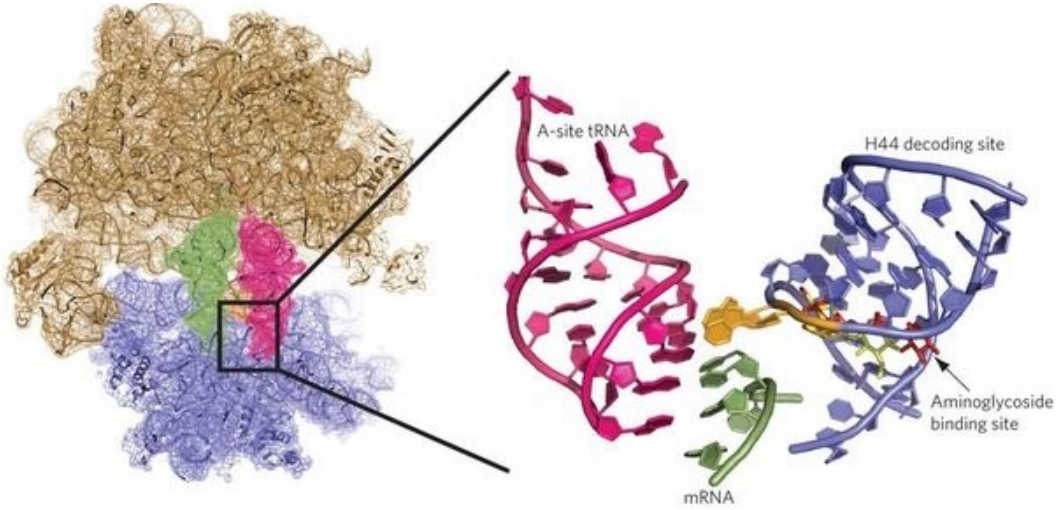
Advances in our understanding of translational read-through enables design of novel small molecules

Target Profile for Read-Through

Eloxx read-through program is pursuing product candidates with the following characteristics:

Activity independent of gene size or complexity of genetic disorder		Molecular scaffold with defined ribosomal effect	Active at all three premature stop codons
Reduces rate of nonsense mediated decay	Restores protein production to a clinically significant level	Acceptable tolerability profile	Suitable for chronic administration

Aminoglycoside Ribosomal Interaction

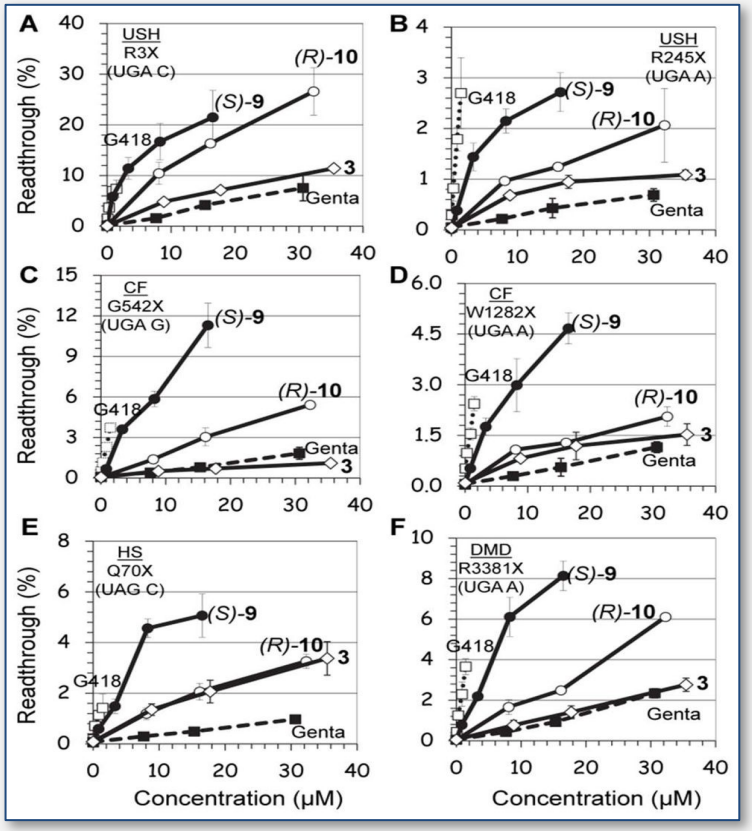


- Well defined molecular interaction with helix 44
- Role in stabilization of tRNA binding at Site A
- Optimizing scaffold by altering interaction with prokaryotic and mitochondrial ribosomes
- Defined tissue penetration and tolerability profile for read-through applications

Aminoglycoside activity observed on single pre-translocation ribosome complexes. Feldman, MB; Terry DS; Altman RB; Blanchard SC. Nature Chemical Biology volume6, pages54–62 (2010)

Discovery of ELX-02

- Novel compounds derived from aminoglycoside scaffold
- Screened for read-through activity on known disease related nonsense mutations
- Reduced mitochondrial inhibition (range 12-140X)
- Reduced prokaryotic ribosomal inhibition



Increased Selectivity towards Cytoplasmic versus Mitochondrial Ribosome Confers Improved Efficiency of Synthetic Aminoglycosides in Fixing Damaged Genes: A Strategy for Treatment of Genetic Diseases Caused by Nonsense Mutation. Kandasamy, K; Atia-Gilkin D; et al. J Med Chem (2012) 55(23):10630-10643

ELX-02 Preclinical Development

CTA (EU) & IND (US) Enabling Studies

- **Functional and anatomic hearing studies**
  - No observation of ototoxicity
- **Histopathology and functional renal studies**
  - Data to date suggest improved NOAEL margin
  - Currently anticipate dosing without adjustment for renal impairment
- **On track for mid-year CTA & IND submissions**

Initiated regulatory pre-IND review of CMC to support planned clinical program

ELX-02 Clinical Development – Phase 1 Studies

CLINICALTRIALS.GOV
Identifier: NCT03292302

A Phase 1a, Randomized, Double-blinded, Placebo-Controlled, Single Dose Escalation Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of ELX-02 in Healthy Adult Volunteers

COMPLETED

CLINICALTRIALS.GOV
Identifier: NCT03309605

A Phase 1, Randomized, Double-Blinded, Placebo-Controlled, Third Party Open, Multiple Dose Escalation, Single Center Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Subcutaneously Administered ELX-02 in Independent Consecutive Cohorts of Healthy Subjects

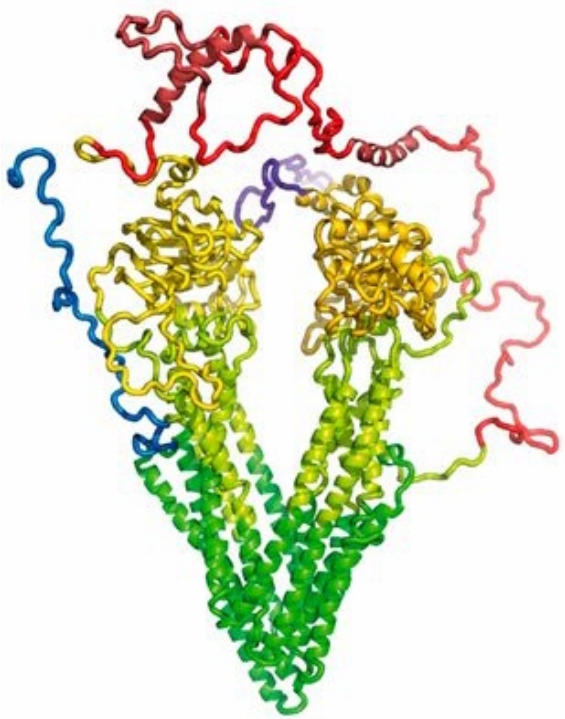
Planned Enrollment: 45

ONGOING

TO DATE:
- No SAE Observed
- No renal or otoacoustic SAE
- Generally well tolerated

Cystic Fibrosis Development Program

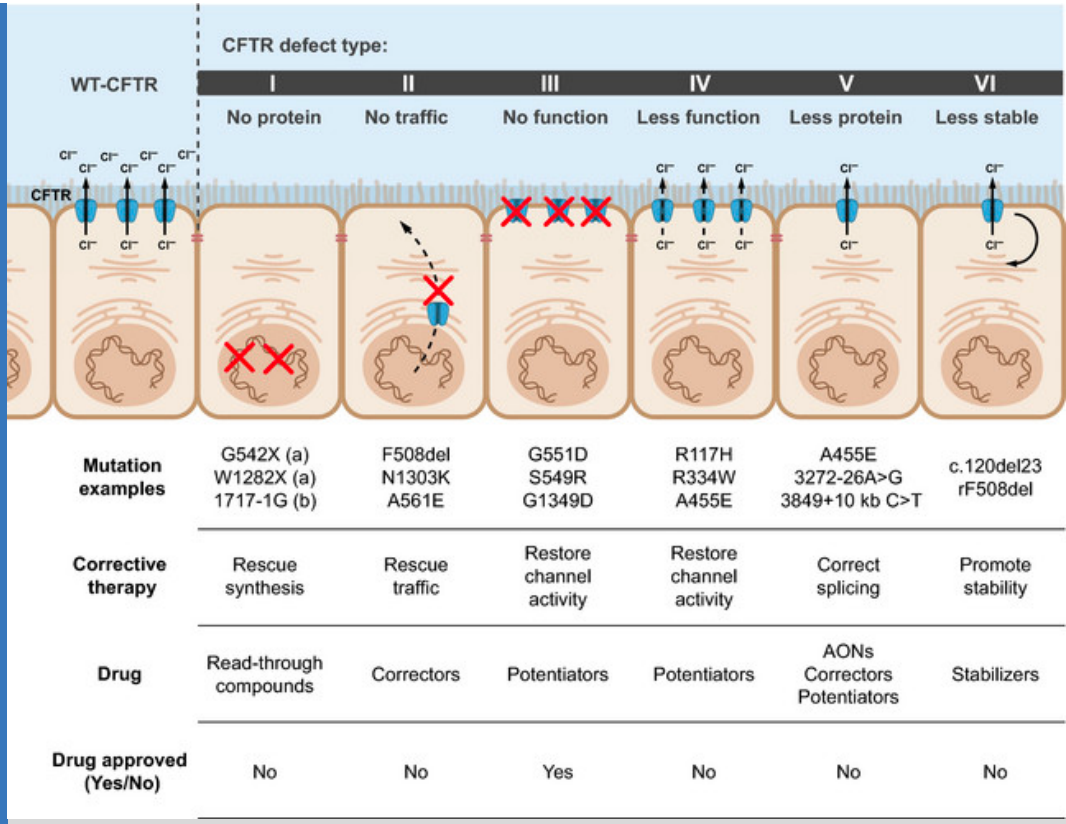
- Systemic rare disease
- Caused by mutations in transmembrane conductance regulator (CFTR)
  - Chloride channel
- Mutations lead to dysregulation in multiple organ systems
- Current standard of care based on molecular chaperones for trafficking and conformation
  - Target Class II – Class V CFTR Defects
  - No currently approved drugs for Class I CFTR Defects
- Currently available data for our investigational drug, ELX-02, suggests the potential for:
  - Active for both homozygous and heterozygous Class I nonsense mutations
  - Increase translational read-through
  - Improve chloride currents in HBEs and organoids
  - Demonstrate synergy with correctors and potentiators in heterozygous population



Zoltan Bozoky et al. PNAS 2013;110:47:E4427-E4436

Cystic Fibrosis: CFTR Molecular Defect

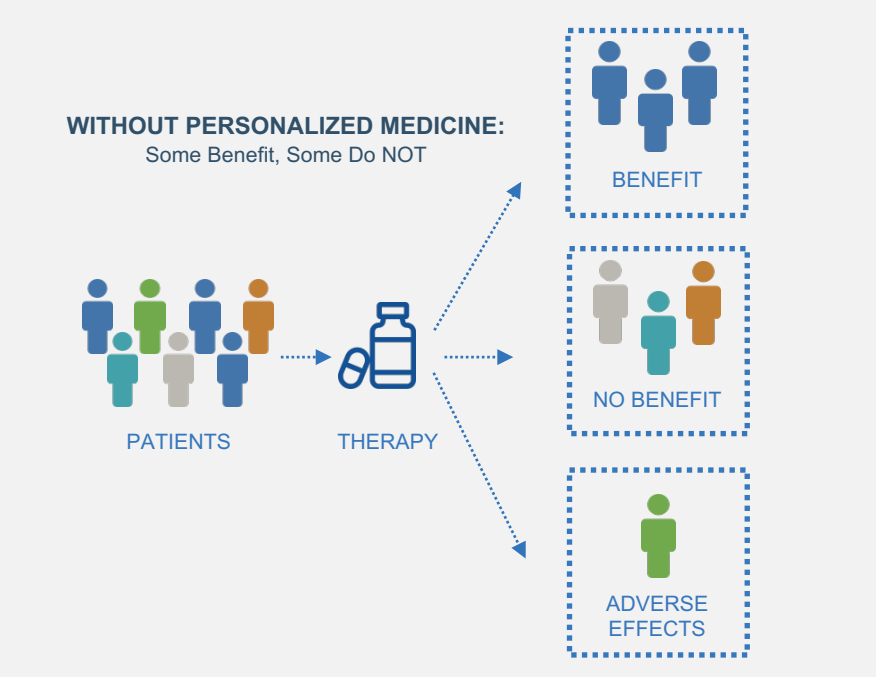
- Premature stop codons or nonsense mutations are Class I
- Estimated that 22% of patients have Class I mutations on one or both CFTR alleles
- The G542X nonsense mutation occurs in 5% of CF patient population
- Eloxx's development path for read-through therapeutics will be focused on the patient subset with diagnosed nonsense mutations

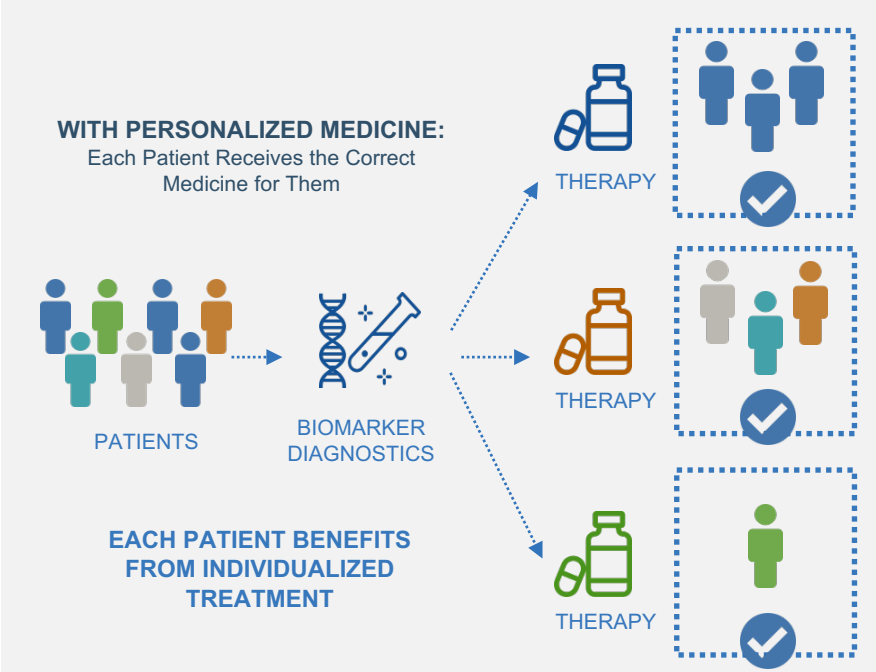


Novel personalized therapies for cystic fibrosis: Treating the basic defect in all patients. Journal of Internal Medicine 277(2) · September 2014

Goals of Cystic Fibrosis Personalized Medicine Approach

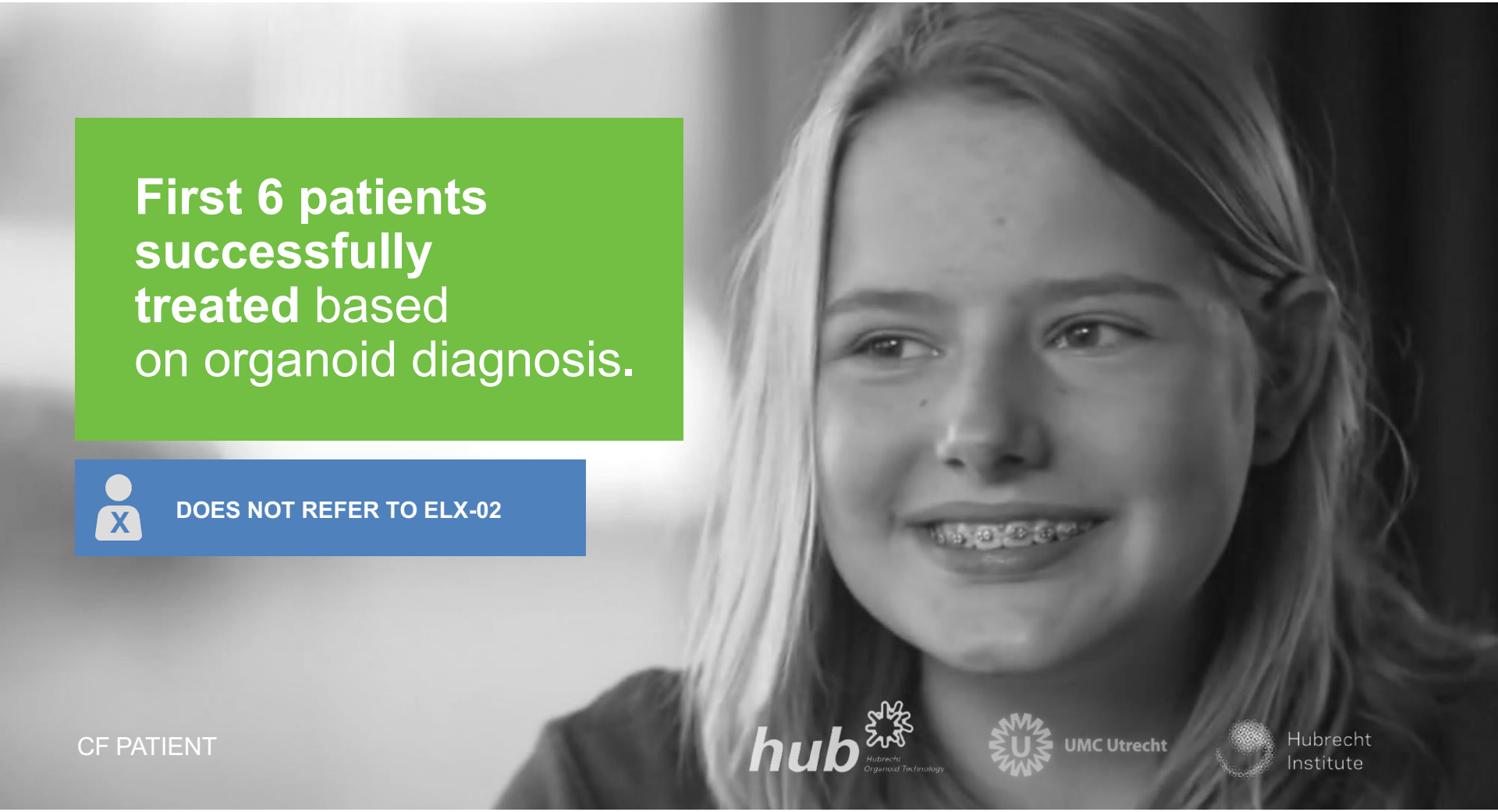
Development path focused on individual's genetic background
(ie, CFTR mutation)





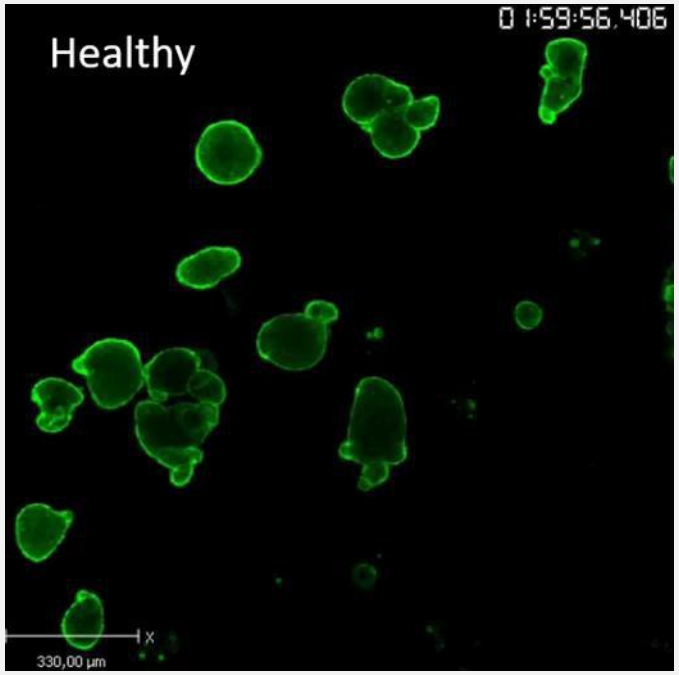
Today most patients have genetic sequence data that could enable personalized treatment

Cystic Fibrosis:
First Organoid Clinical Success

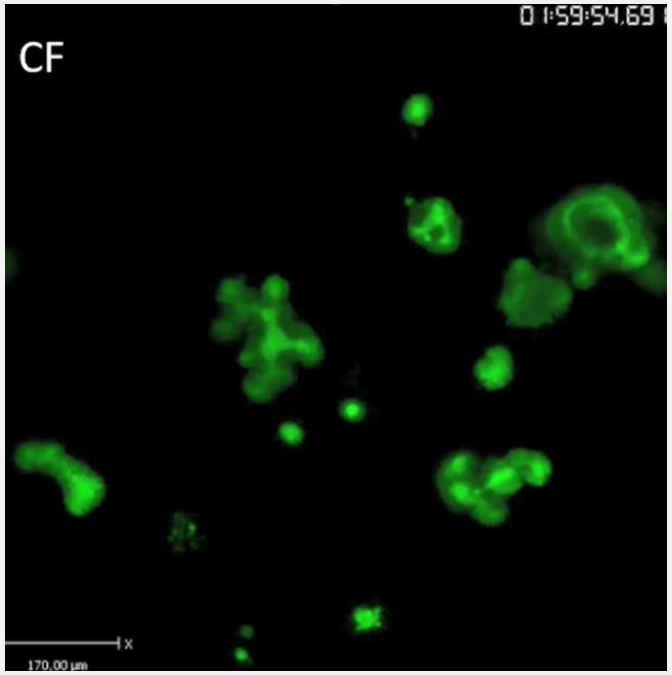


Organoids For Cystic Fibrosis Screening

A CF assay on cystic fibrosis patient organoids



Healthy CFTR activation:
Swelling of Organoids

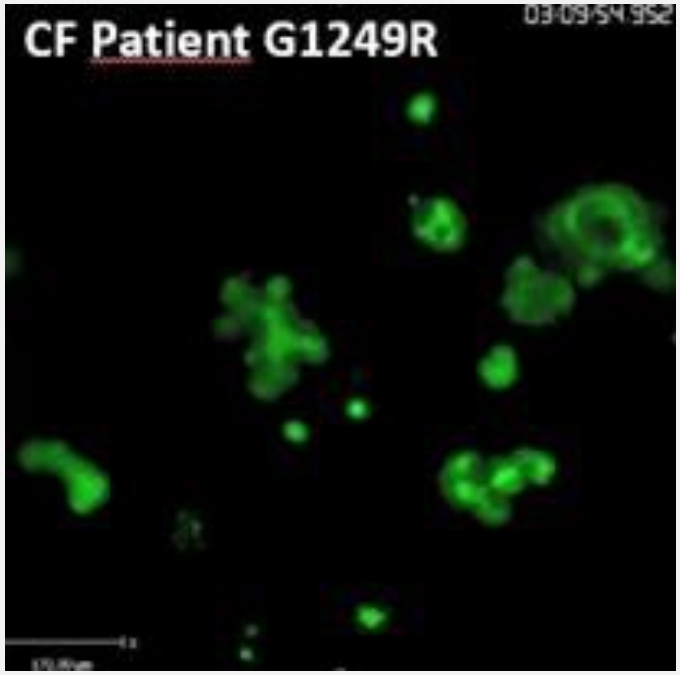


CF mutated CFTR activation:
No-Swelling of Organoids

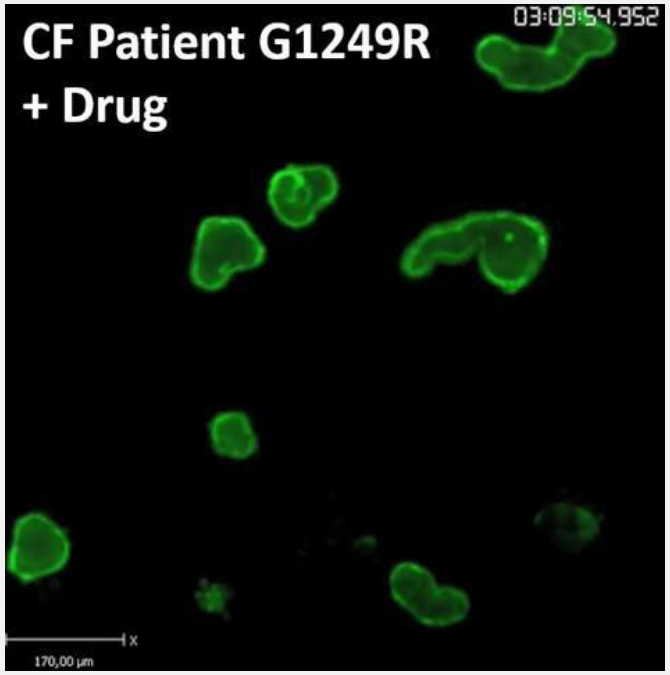
Organoids Pre-clinical Patient Stratification

Potential Use To Define Clinical Trial Populations

A CF swelling assay on cystic fibrosis patient organoids



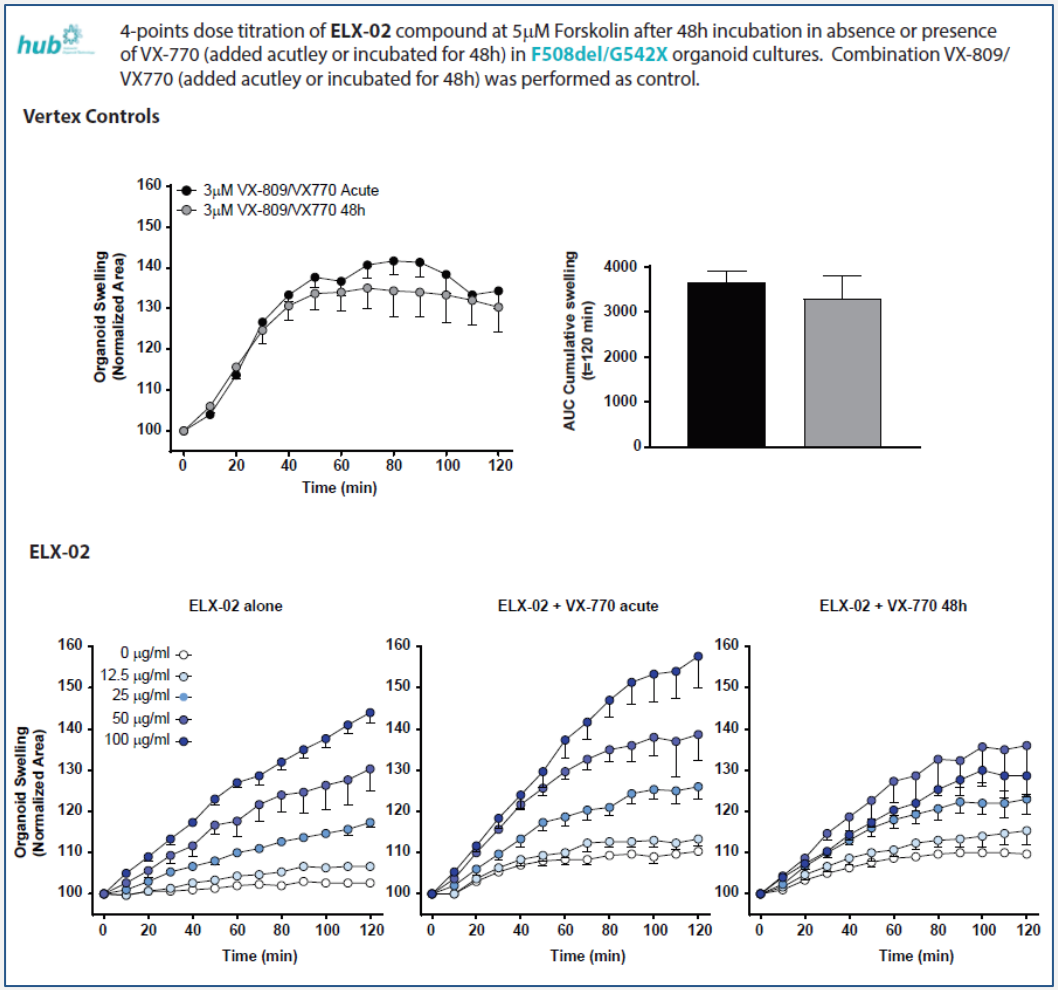
Patient Organoid without drug treatment:
No Swelling of Organoids



Patient Organoid with drug treatment:
Swelling of Organoids

Heterozygous nonsense mutations

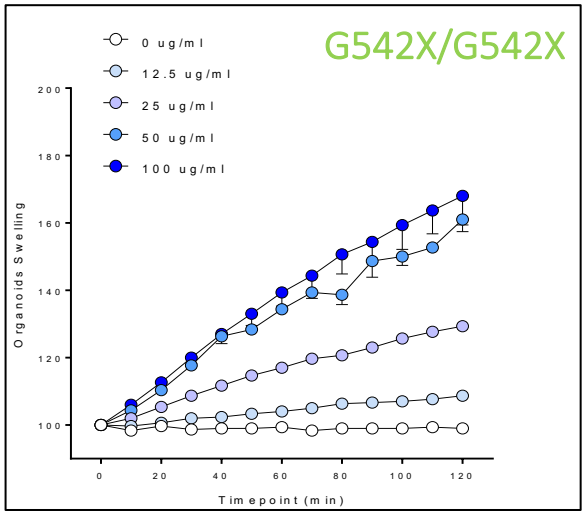
First investigational read-through agent to demonstrate in vitro activity in organoid cultures

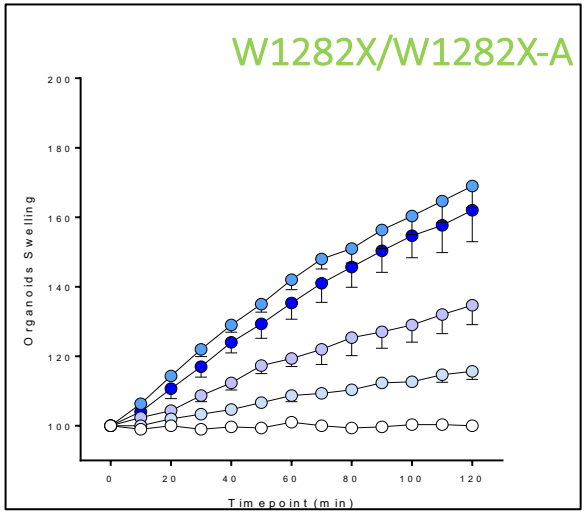


Homozygote nonsense mutations

First investigational read-through agent to demonstrate in vitro activity in organoid cultures

- Early-stage data involve key homozygous nonsense mutations
  - G542X prevalence estimated at 5% of CF population
  - W1282X prevalence est. at 4% of CF population
- This testing in a limited number of in vitro organoid cultures suggests organoid response to increasing exposure to our drug candidate ELX-02
  - Dose-proportional response
  - Pronounced swelling
- Organoid responses are considered important contributor to clinical trial design
  - High unmet medical need population
  - Demonstrate potential for clinical response
- Data to be submitted for scientific presentation
  - Additional homozygous and heterozygous response data
  - Evaluation of in vitro response in organoid cultures in combinations with correctors and/or potentiators



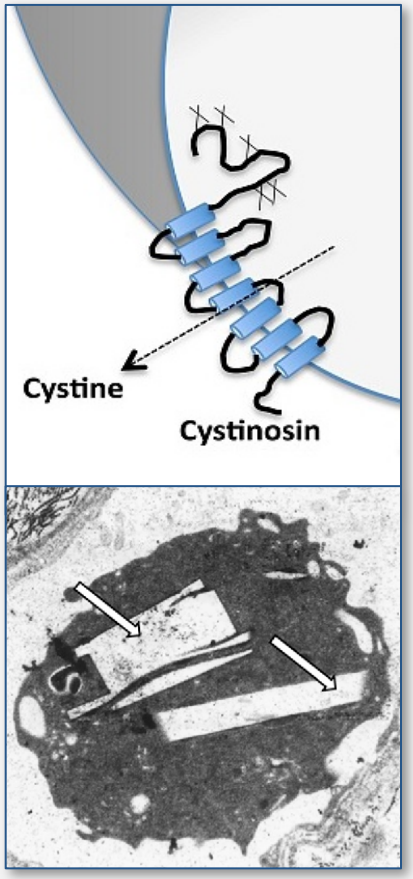


ELX-02 Cystic Fibrosis Next Steps

- Jan 2018 Pre-CTA (Belgium) Regulatory Meeting
- On track for mid-2018 CTA (Belgium) Submission
- Targeting 4Q 2018 for FPFV Phase 2 Study

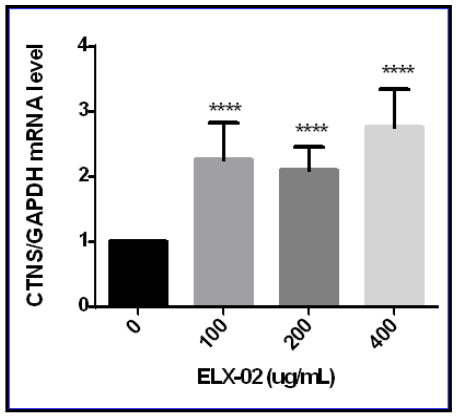
Cystinosis Development Program

- Ultra-rare lysosomal storage disease
- Caused by mutations in cystinosin (CTNS)
  - Cysteine efflux channel
- Cystine lysosomal accumulation causes manifestations of disease
- The current standard of care, Cysteamine acts within the lysosome to convert cystine into forms which can exit the lysosome via cysteine transport pathways.
- W138X most common nonsense mutation is estimated to represent 1/3 of patient population
- Currently available data on our investigational drug candidate, ELX-02, suggest the potential to:
  - Increase translational read-through
  - Reduce NMD
  - Restore CTNS mRNA to near normal levels
  - Lower cystine accumulation in vitro and in vivo



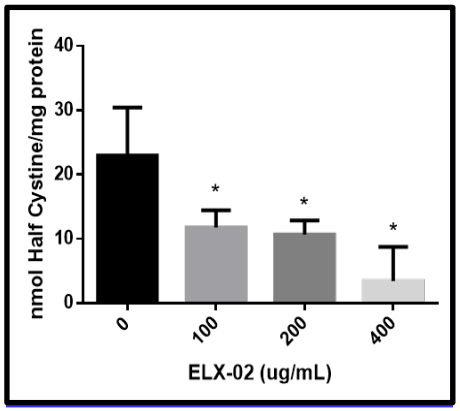
ELX-02 Preclinical Cystinosis

IN VITRO MODEL
CTNS$^{W138X/W138X}$
FIBROBLASTS



Nonsense-mediated mRNA decay

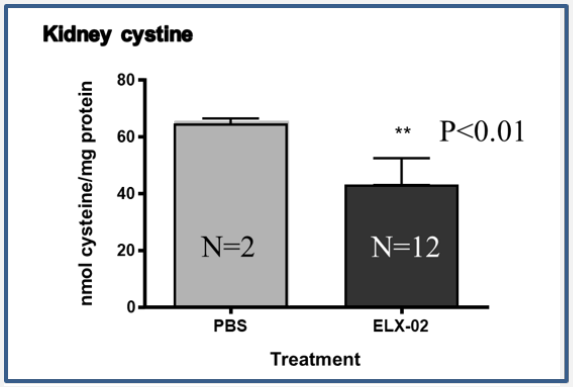
In vitro model suggests ELX-02 reduces nonsense mediated decay (NMD)



Cystine Accumulation

In vitro model suggests ELX-02 restores Cystinosin transporter function

ELX-02 Animal Model Cystinosis



Cystine Accumulation

21 Days of Biweekly Administration of Investigational Drug Candidate ELX-02 Significantly Reduced Kidney Cystine Levels

14TH ANNUAL
WORLDSymposium™
February 5-9, 2018
We're Organizing Research on Lysosomal Diseases

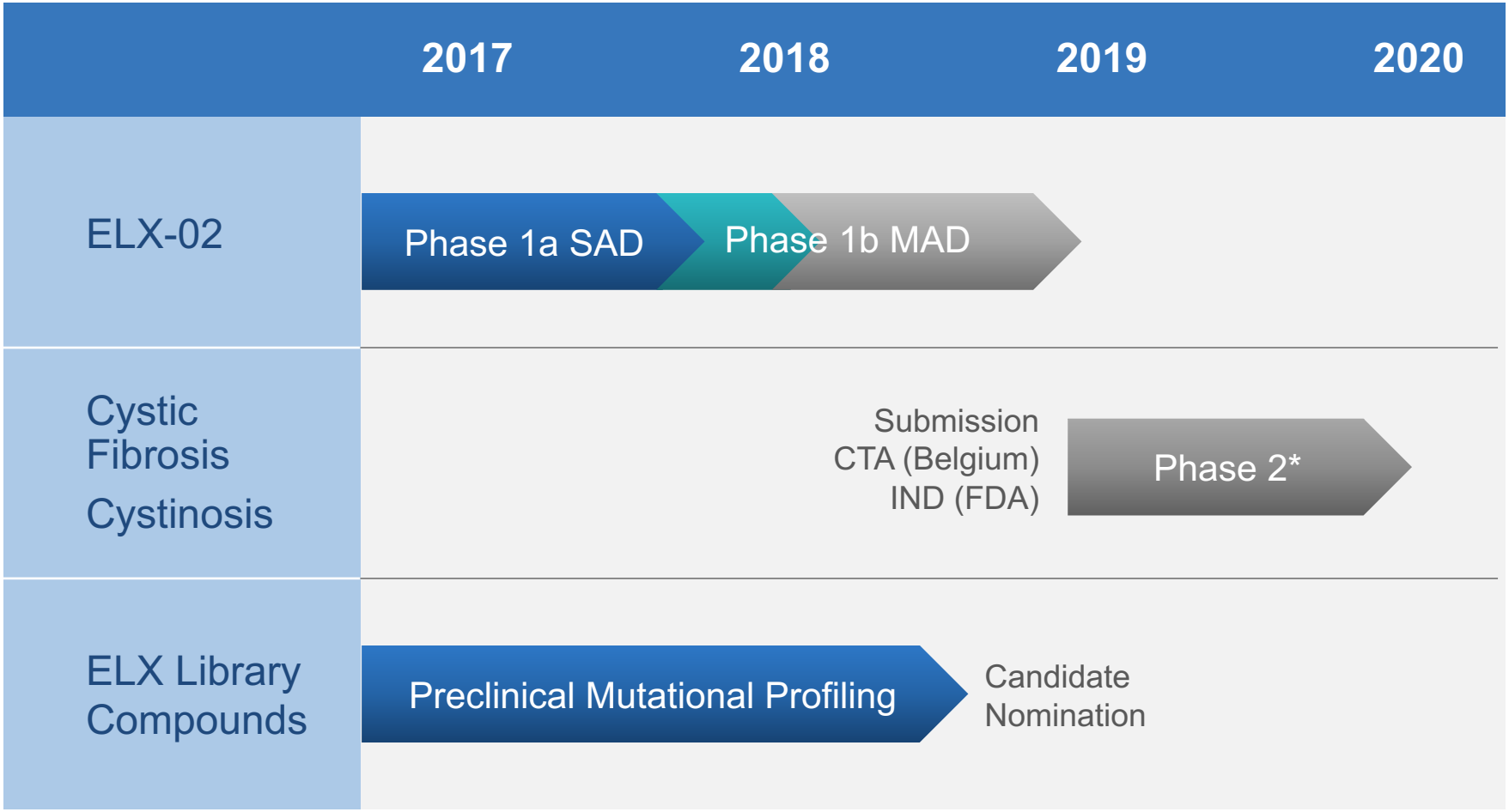
CTNS$^{Y226X/Y226X}$ knock-in

Dr Paul Goodyer
McGill University

ELX-02 Cystinosis Next Steps

- Dec 2017 Pre-IND FDA (Written Response)
- On track for mid-2018 IND Submission in US
- Targeting 4Q2018 for FPFV Phase 2 Study

Our Current Development Pipeline



ELX-02 and the ELX Library Compounds are investigational agents and have not been approved for use by any regulatory agency

**Subject to Regulatory Review of CTA and IND respectively*

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Thank you.

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