Eloxx Pharmaceuticals

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

Investor Presentation
February 2018

Forward-Looking Statements

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Eloxx Pharmaceuticals Highlights

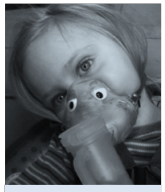
Leading Read Through Company	Clinical stage biopharmaceutical company developing novel small molecule medicines designed to treat genetic diseases by restoring the production of proteins from genes with nonsense mutations
Experienced Management	Management team with established track record of successful 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.
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

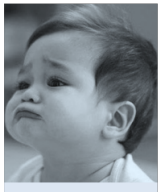
Highly Experienced Leadership Team

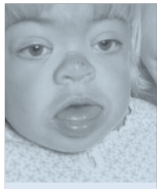
Robert Ward Chairman and CEO	Radius AstraZeneca	**Pedro Huertas, MD, PhD** CMO	Pfizer Shire
Gregory Weaver CFO	Prometic ORYZON	**John van Duzer, Ph.D.** VP CMC	Celgene Acetylon Pharmaceuticals, Inc.
Barbara Ryan Investor Relations	Radius Deutsche Bank	**Neil Sharpe, Ph.D.** VP Translational Sci.	Biogen 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 product of essential proteins
- Translational read through restores the production of full length proteins by overcoming the premature stop codon and nonsense mediated decay

Aminoglycosides first showed read-through activity in nonsense mediated diseases

Aminoglycosides tolerability profile has limited suitability for read through treatment of serious genetic diseases

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

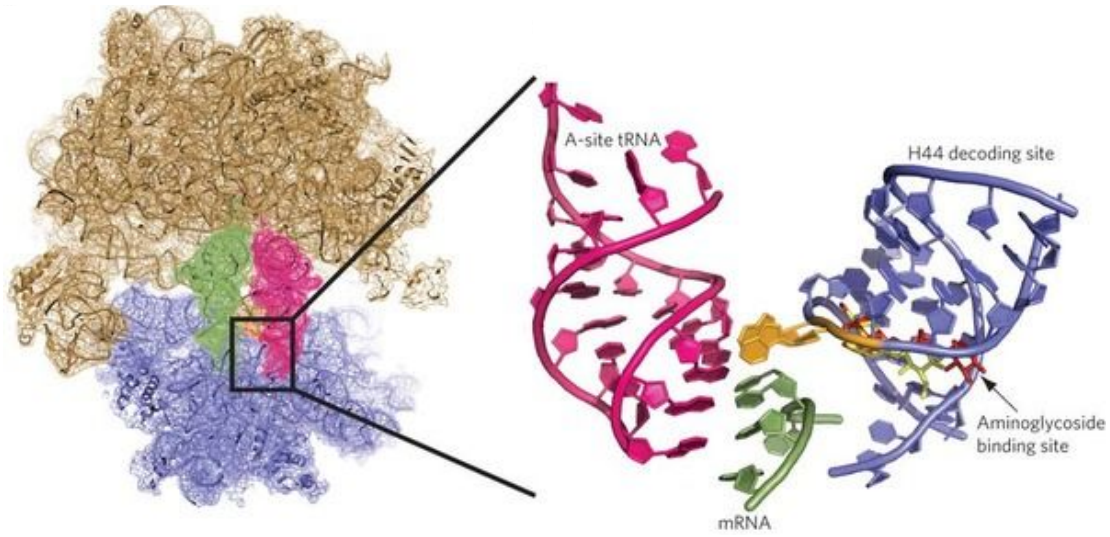
ELO

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

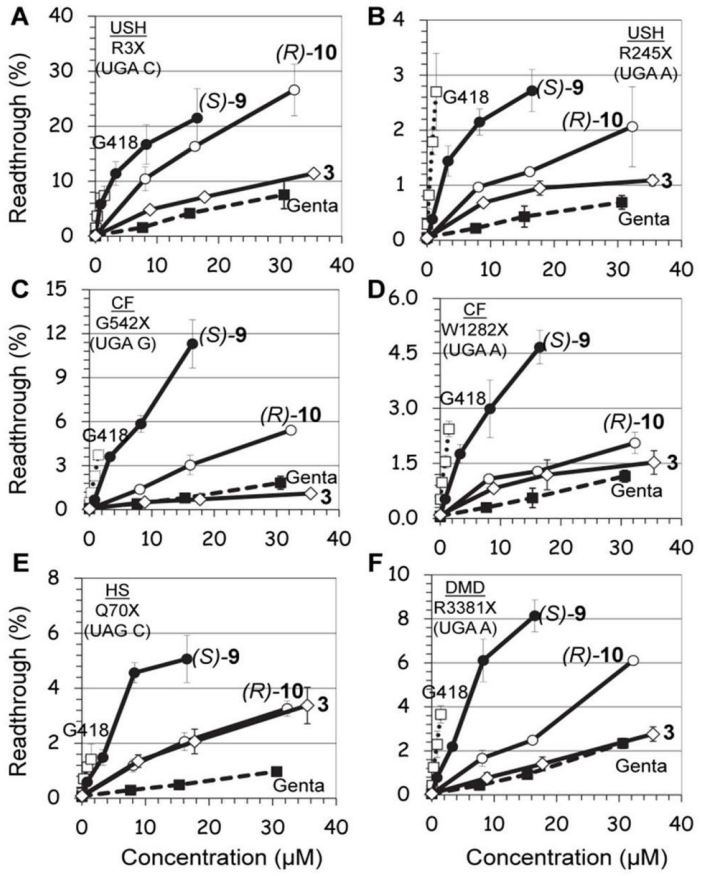


- Well defined molecular interaction with helix 44
- Role in stabilization of tRNA binding at Site A
- Optimizing scaffold by altering interaction with prokaryotic and mitochondrial ribosomes
- Defined tissue penetration and tolerability profile for read-through applications

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

- IND Enabling Studies
  - Functional and anatomic hearing studies
    - No observation of ototoxicity
  - Histopathology and functional renal studies
    - Indication of improved NOAEL margin
    - Currently anticipate dosing without adjustment for renal impairment
  - On track for mid-year submission
- Initiated regulatory pre-IND review of CMC to support planned clinical program

ELX-02 Clinical Development

ClinicalTrials.gov Identifier: NCT03292302

Completed

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

To Date:
No SAE Observed
No renal or otoacoustic SAE
Generally well tolerated

ClinicalTrials.gov Identifier: NCT03309605

Ongoing

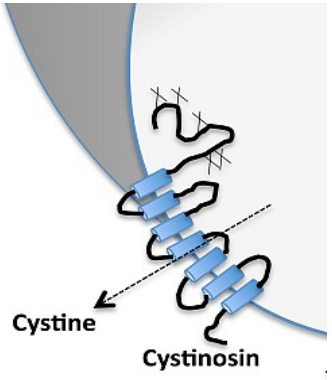
A Phase 1, Randomized, Double-Blinded, Placebo-Controlled, Third Party Open, Multiple Dose Escalation, Single Center Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Subcutaneously Administered ELX-02 in Independent Consecutive Cohorts of Healthy Subjects

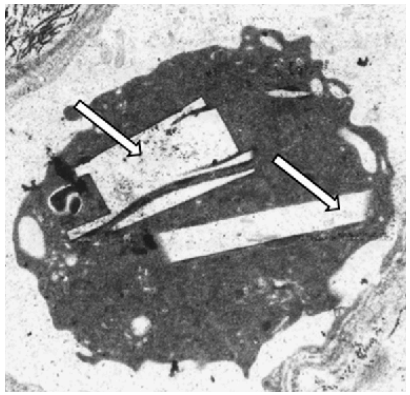
Planned Enrollment 45

ELO

Cystinosis Development Program

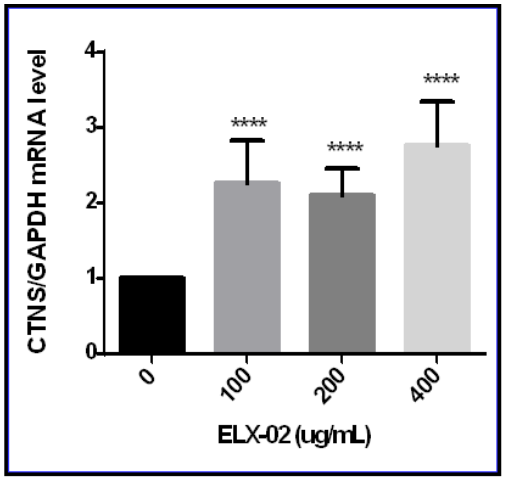
- Ultra-rare lysosomal storage disease
- Caused by mutations in cystinosin (CTNS)
  - Cysteine efflux channel
- Cystine lysosomal accumulation causes manifestations of disease
- It is generally recognized that the current standard of care (cysteamine administration) stimulates alternative transport pathway
- W138X most common nonsense mutation represents 1/3 of patient population
- ELX-02 currently available data indicate 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

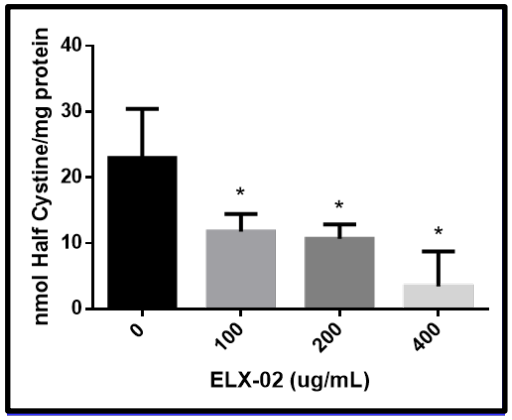
In vitro model indicates ELX-02 reduces nonsense mediated decay (NMD)



Nonsense-mediated mRNA decay

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

In vitro model indicates ELX-02 restores Cystinosin transporter function



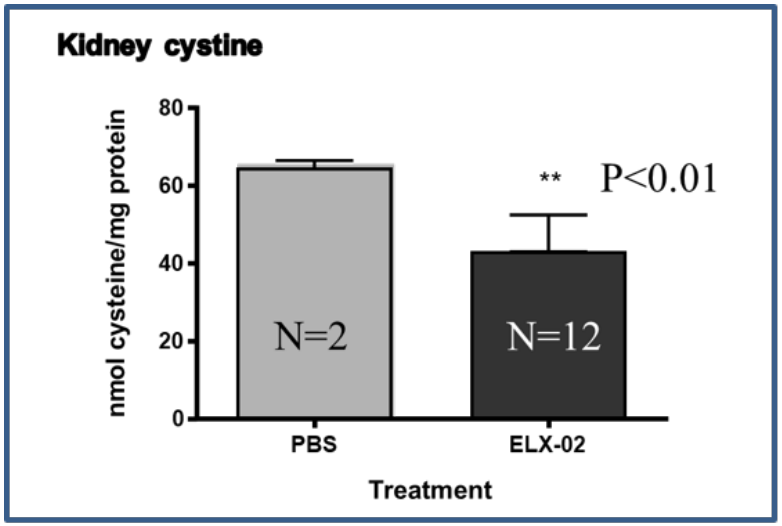
Cystine Accumulation

ELX-02 Animal Model Cystinosis

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

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

Dr Paul Goodyer
McGill University



Cystine Accumulation

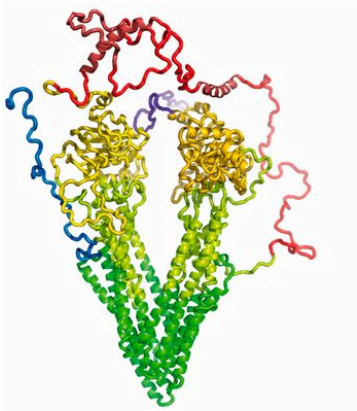
21 Days of Biweekly
ELX-02 Administration
Significantly Reduced
Kidney Cystine Levels

ELX-02 Cystinosis Next Steps

- √ Dec 2017 Pre-IND FDA Discussion
- On track for mid-2018 IND Submission in US
- Targeting 4Q 2018 for FPFV Phase 2 Study

Cystic Fibrosis Development Program

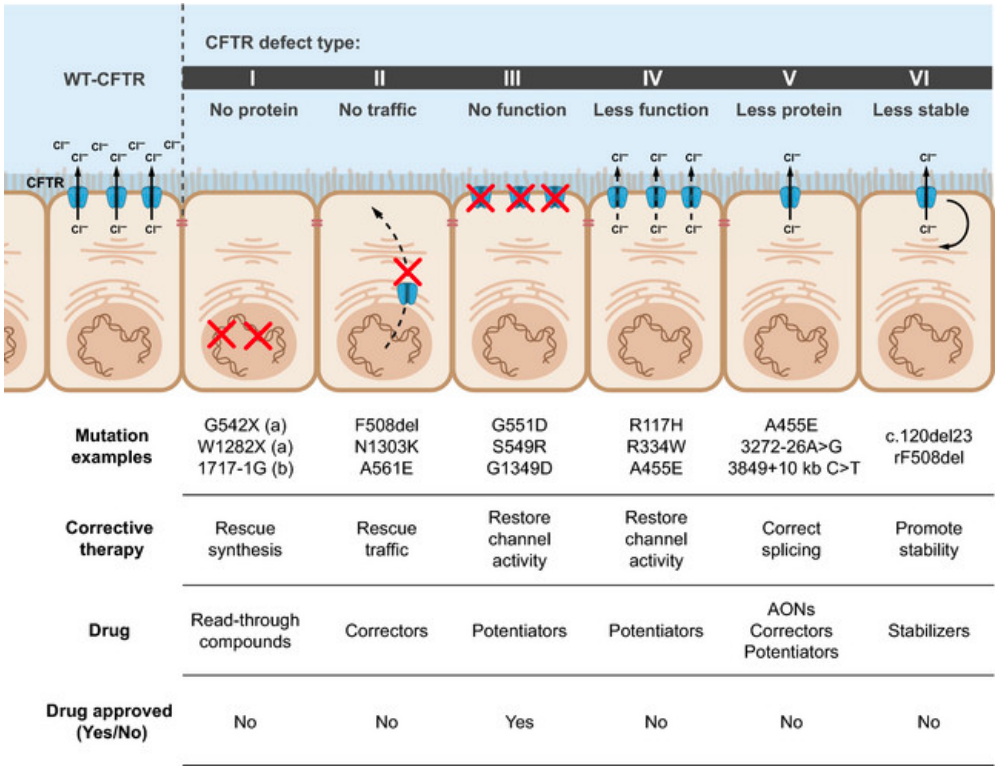
- Systemic rare disease
- Caused by mutations in transmembrane conductance regulator (CFTR)
  - Chloride channel
- Mutations lead to dysregulation in multiple organ systems
- Current standard of care based on molecular chaperones for trafficking and conformation
- G542X most common nonsense mutation represents 5% of patient population
- ELX-02 currently available data indicates the potential to:
  - ✓ 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 1
- There are currently no approved therapies for Class 1
- G542X represents approximately 5% of the total CF patient population
- Eloxx's development path for read-through therapeutics will be focused on the patient subset with diagnosed nonsense mutations

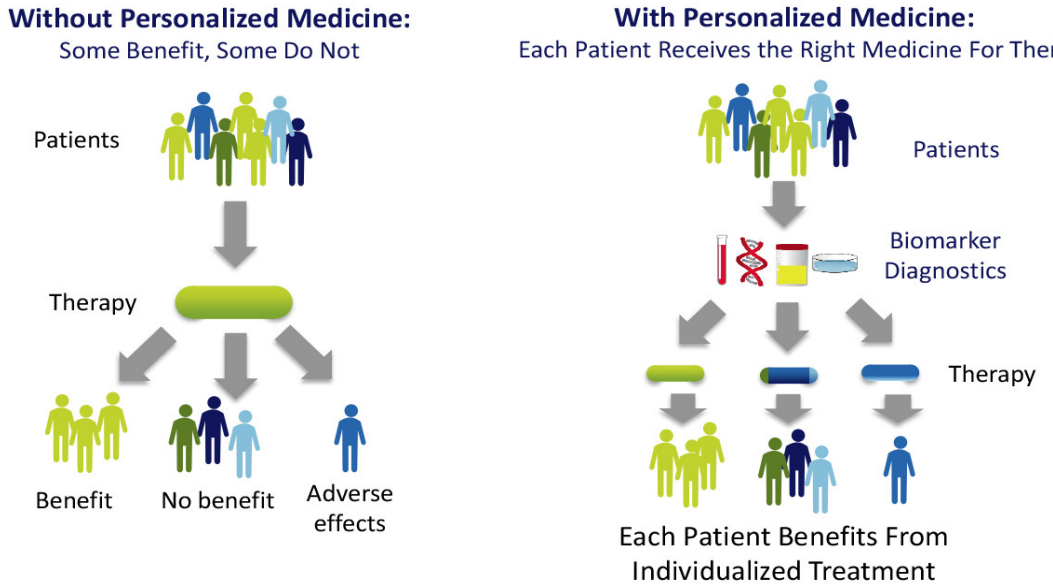


	I	II	III	IV	V	VI
Mutation examples	G542X (a) W1282X (a) 1717-1G (b)	F508del N1303K A561E	G551D S549R G1349D	R117H R334W A455E	A455E 3272-26A>G 3849+10 kb C>T	c.120del23 rF508del
Corrective therapy	Rescue synthesis	Rescue traffic	Restore channel activity	Restore channel activity	Correct splicing	Promote stability
Drug	Read-through compounds	Correctors	Potentiators	Potentiators	AONs Correctors Potentiators	Stabilizers
Drug approved (Yes/No)	No	No	Yes	No	No	No

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

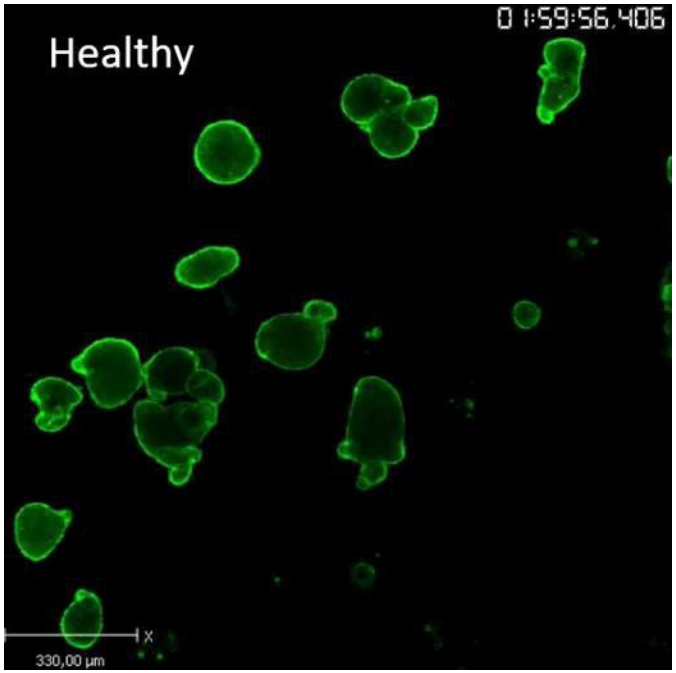
First 6 patients successfully treated based on organoid diagnosis.

Does not refer to ELX-02

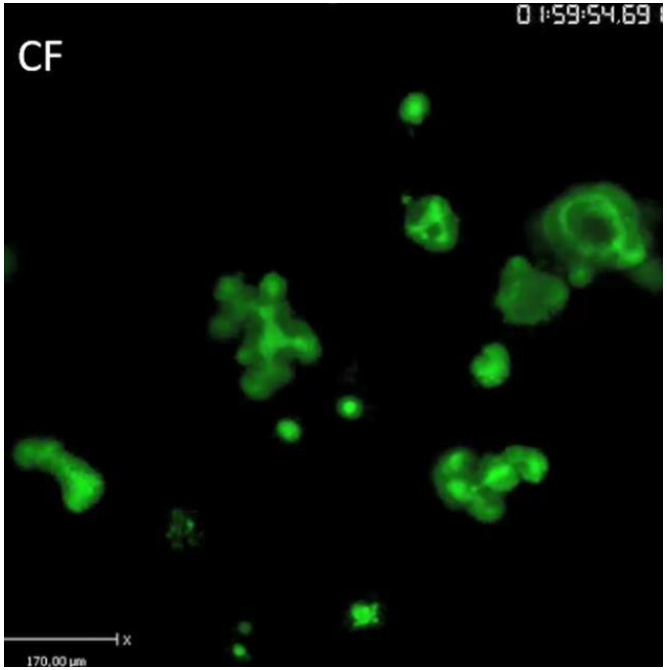
CF patient

Organoids For Cystic Fibrosis Screening

A CF assay on cystic fibrosis patient organoids



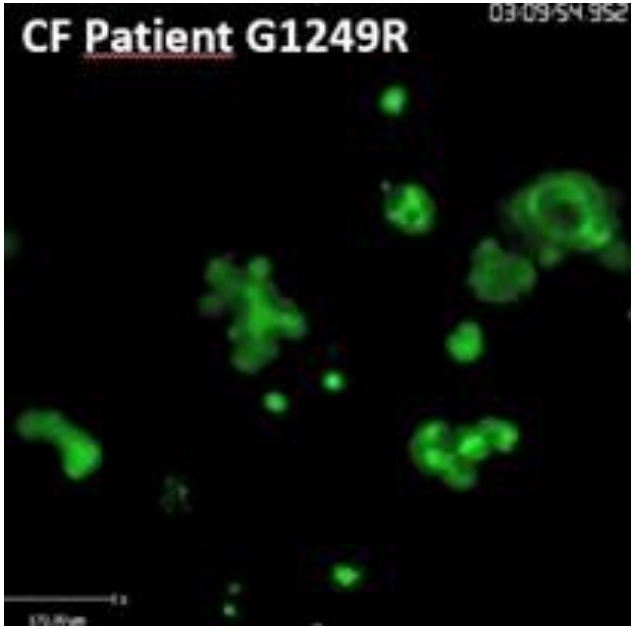
Healthy CFTR activation:
Swelling of Organoids



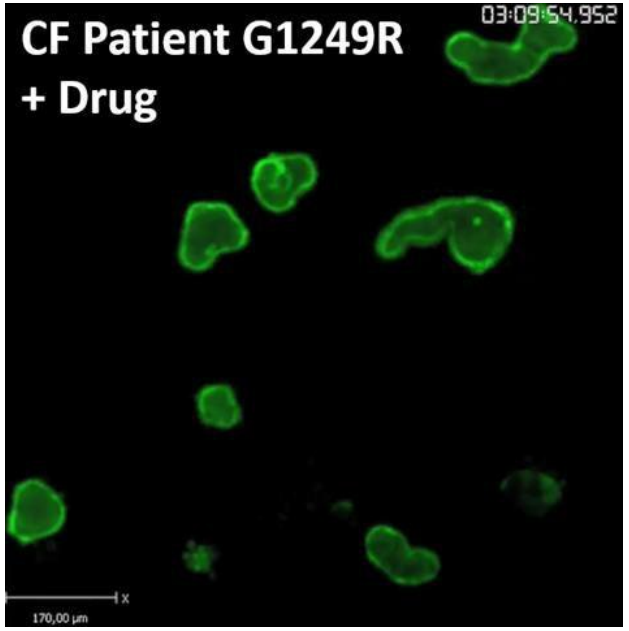
CF mutated CFTR activation:
No-Swelling of Organoids

Organoids Pre-clinical Patient Stratification Can Be Used To Define Clinical Trial Populations

A CF swelling assay on cystic fibrosis patient organoids



Patient Organoid without drug treatment:
No Swelling of Organoids

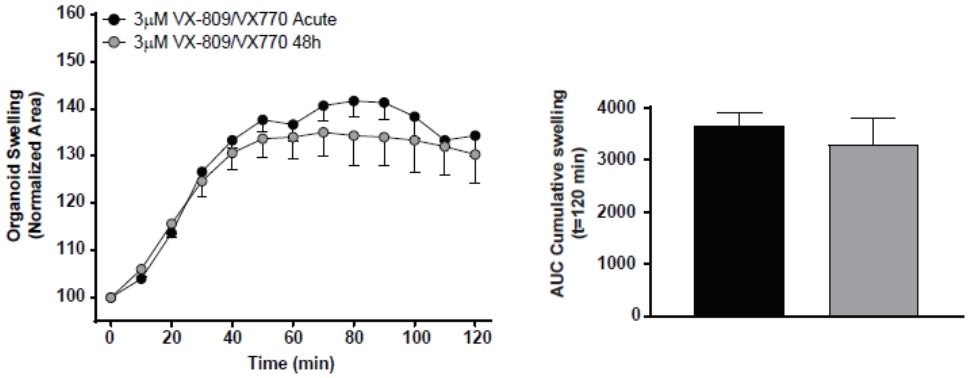


Patient Organoid with drug treatment:
Swelling of Organoids

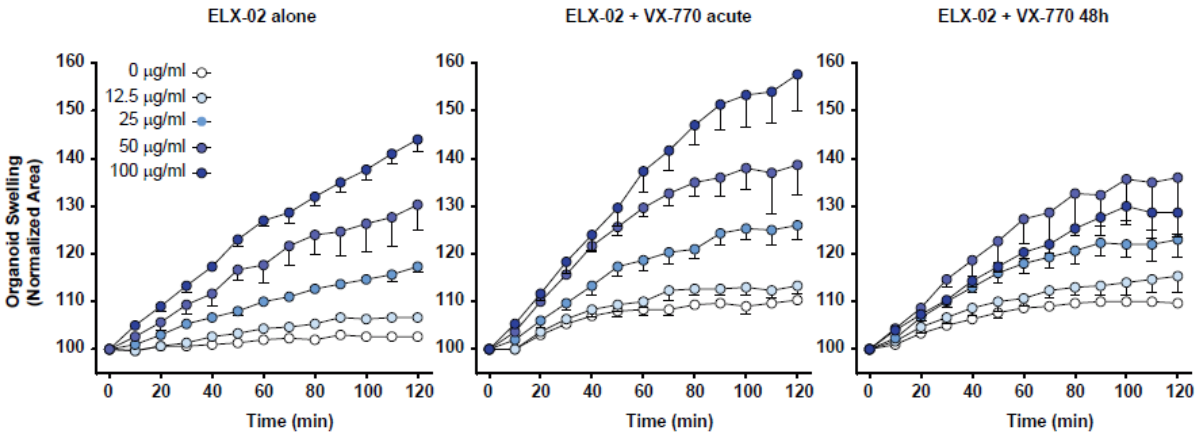
ELX-02 Example Organoid Results

4-points dose titration of **ELX-02** compound at 5μM Forskolin after 48h incubation in absence or presence of VX-770 (added acutley or incubated for 48h) in **F508del/G542X** organoid cultures. Combination VX-809/ VX770 (added acutley or incubated for 48h) was performed as control.

Vertex Controls



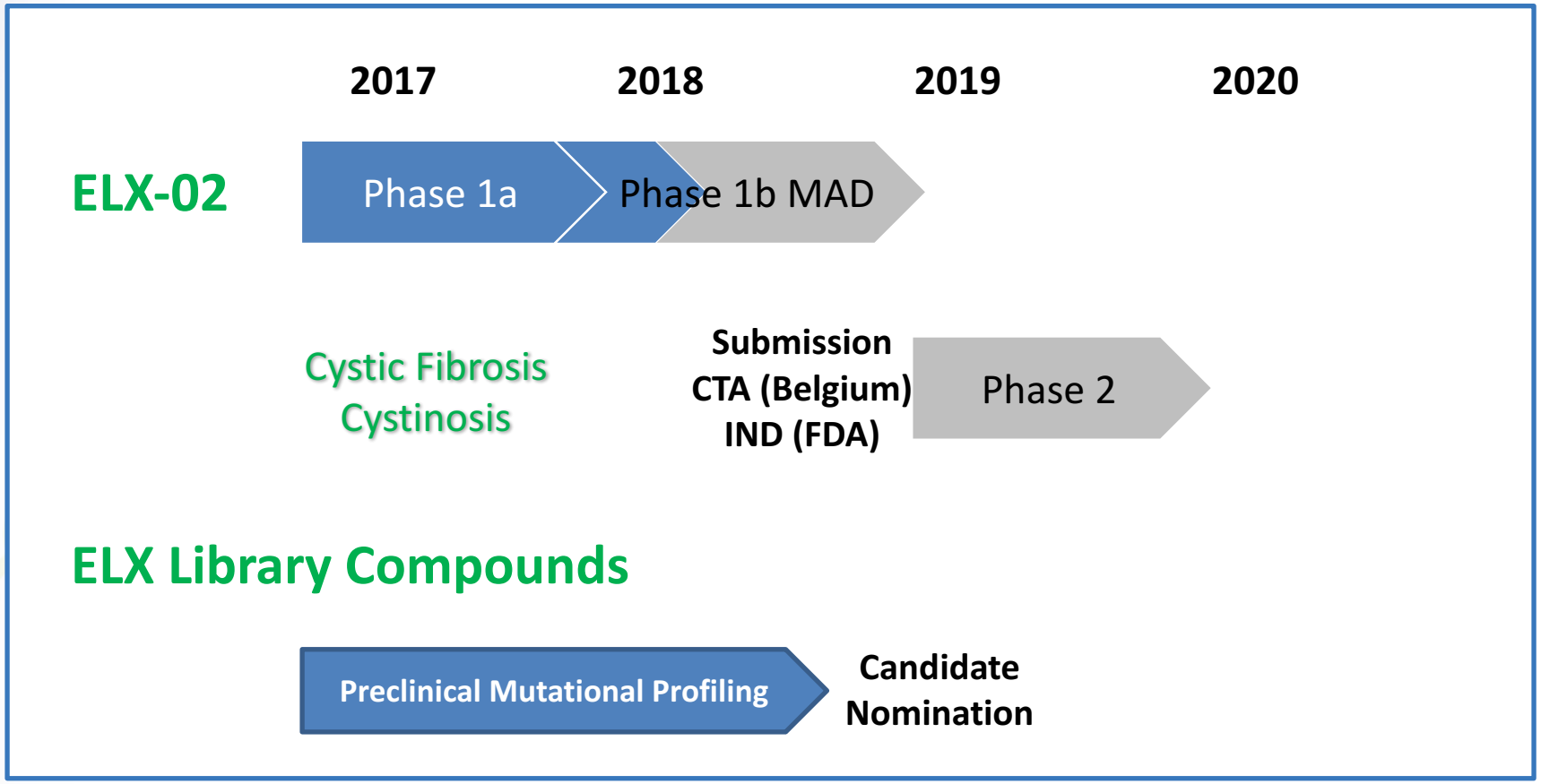
ELX-02



ELX-02 Cystic Fibrosis Next Steps

- √ Jan 2018 Pre-CTA (Belgium) Regulatory Meeting
- On track for mid-2018 CTA (Belgium) Submission
- 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

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March 20
FY2017
Earnings
Call

Suntrust 4th Annual Orphan Drug Day Feb 13, 2018
Cowen 38th Annual Health Care Conference March 12, 2018

Thank you!