Eloxx Pharmaceuticals

ELX-02 increases full-length *CFTR* mRNA through nonsense mediated decay interruption

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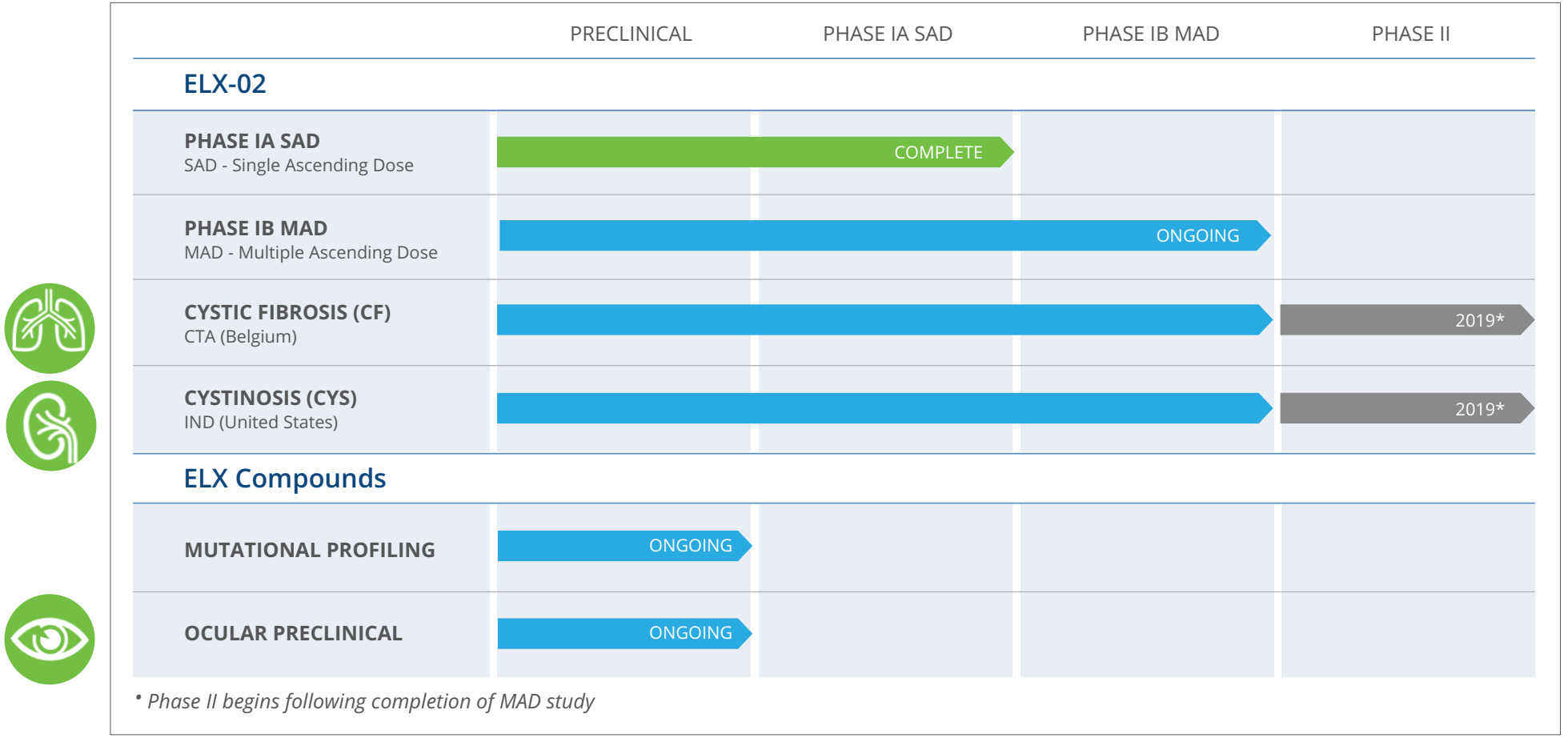
Forward-Looking Statements

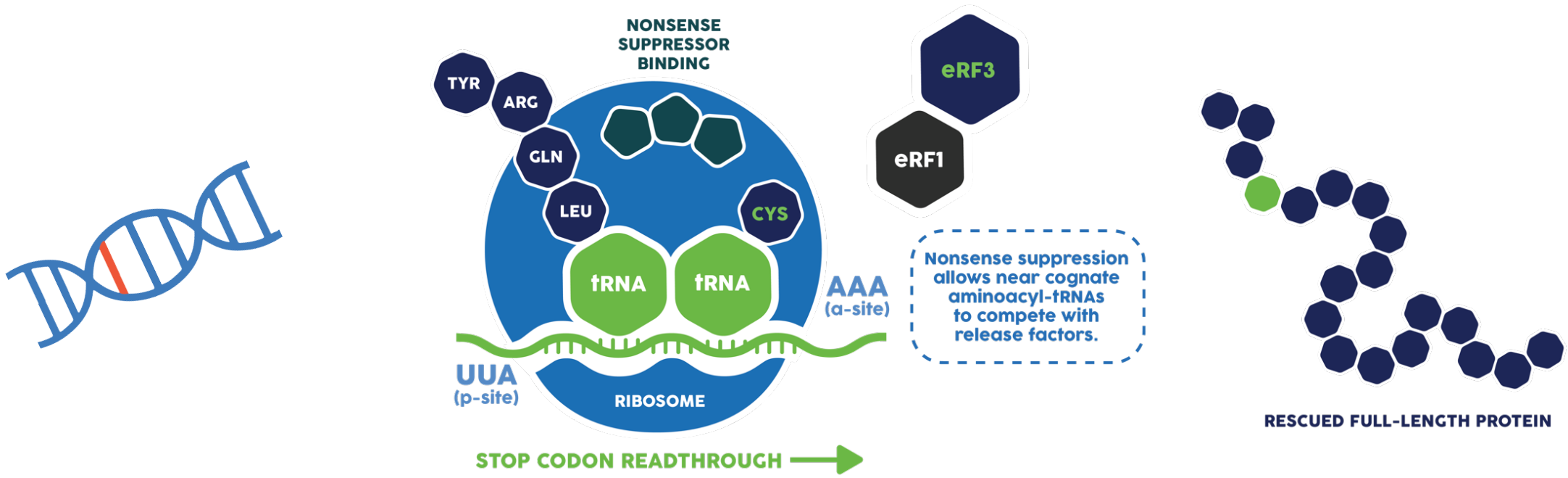
This presentation contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking 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 Pipeline: Targeting Nonsense Allele Genotypes for Rare Diseases



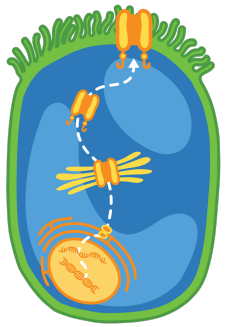
• *Phase II begins following completion of MAD study*

Eukaryotic Ribosomal Selective Glycosides (ERSGs) Nonsense Mutation Suppressors Rescue Full-Length Protein

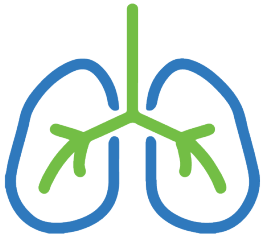


ELX-02: ERSG In Development For Nonsense Mediated Cystic Fibrosis

- ELX-02 is a small molecule that permits read-through of nonsense mutations
  - Defined interaction with the ribosome
  - High selectivity for the eukaryotic cytoplasmic ribosome relative to mitochondrial ribosome

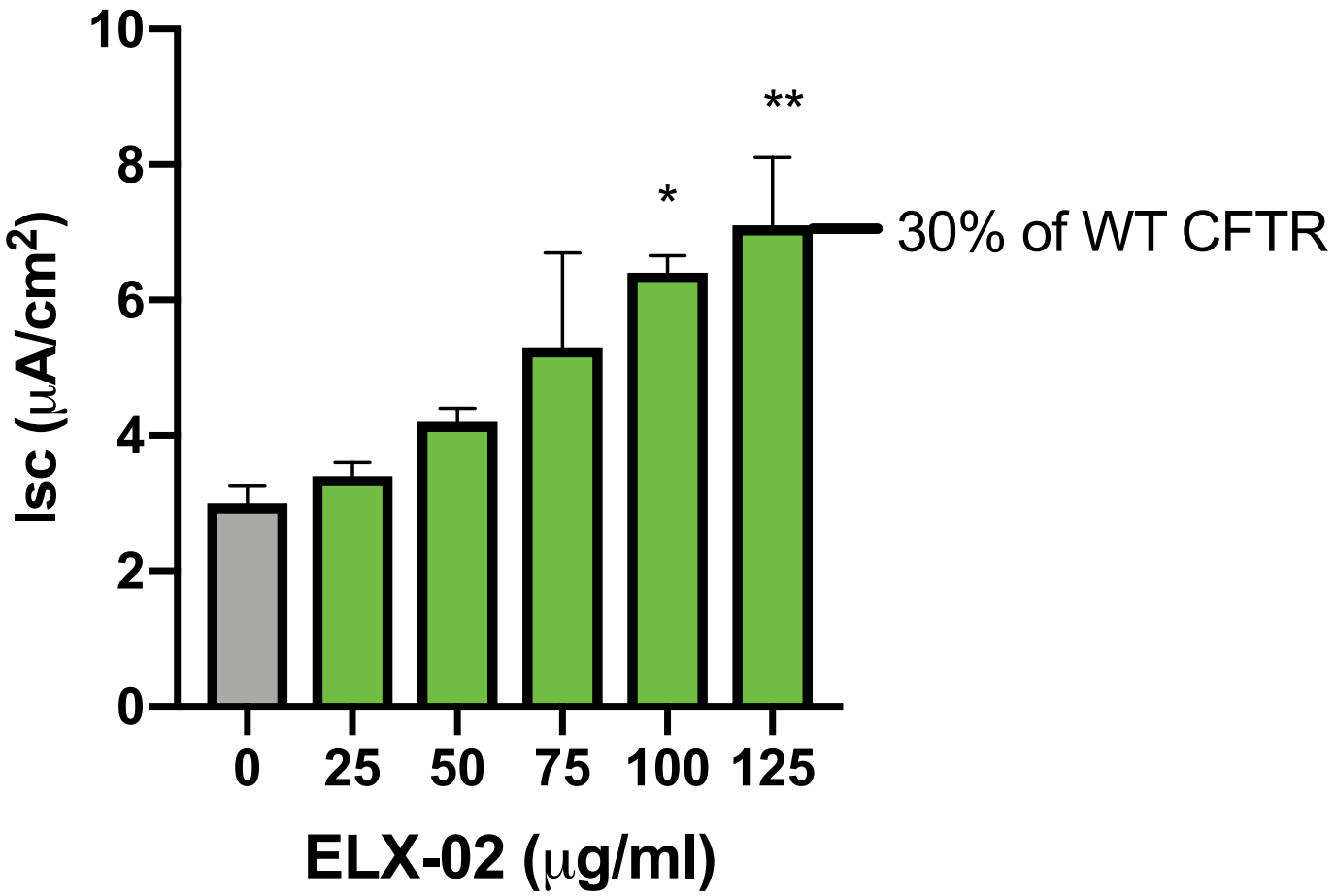


- ELX-02 demonstrates read-through in multiple cystic fibrosis model systems
  - Pronounced *CFTR* read-through demonstrated in plasmid, HBE, FRT, transgenic mice and patient-derived organoids
  - Significant read-through demonstrated for *G542X*, *W1282X*, *R553X*, *R1162X*, and *E60X* alleles representing over 75% of nonsense population
  - Defined MOA: Demonstrated significant increases in CFTR function, protein and *mRNA*



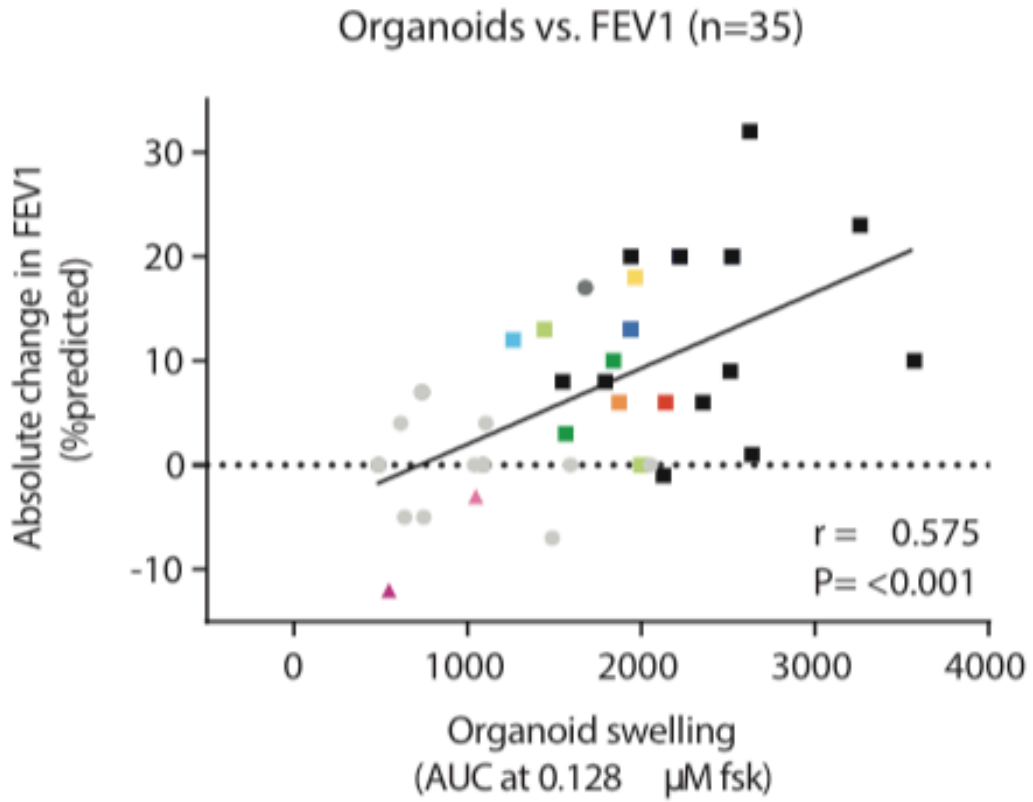
- ELX-02 is progressing to Phase 2 clinical studies
  - Phase 2 focus on patients with *G542X* genotype
  - Planned topline patient data will be reported in 2019

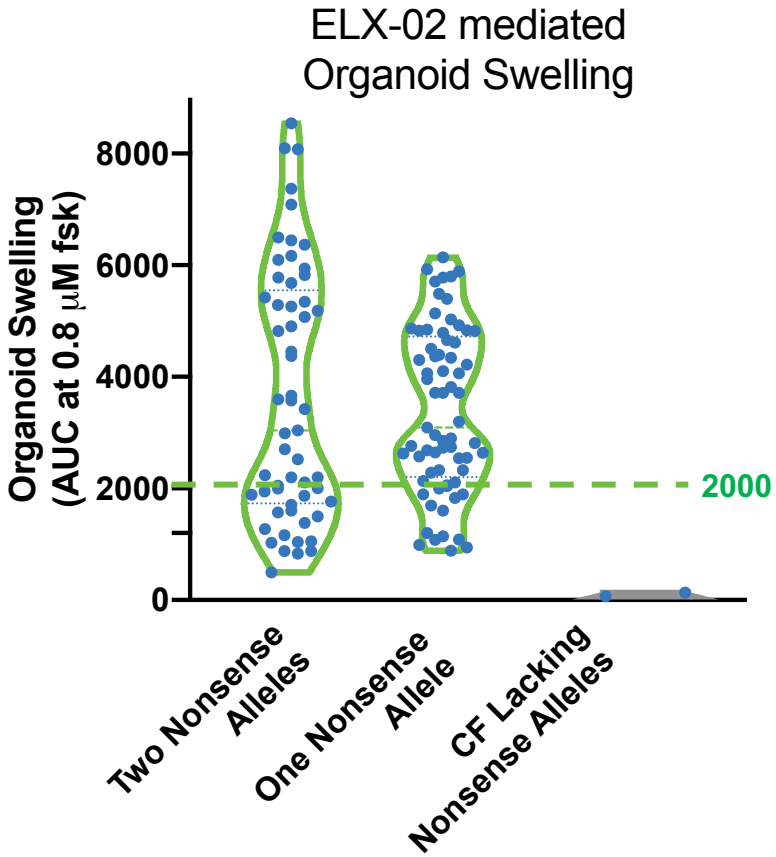
ELX-02 Induces CFTR Rescue in *G542X/F508del* Human Bronchial Epithelial Cells



*p<0.05, **p<0.01
HBE cells were incubated for 2 days with ELX-02

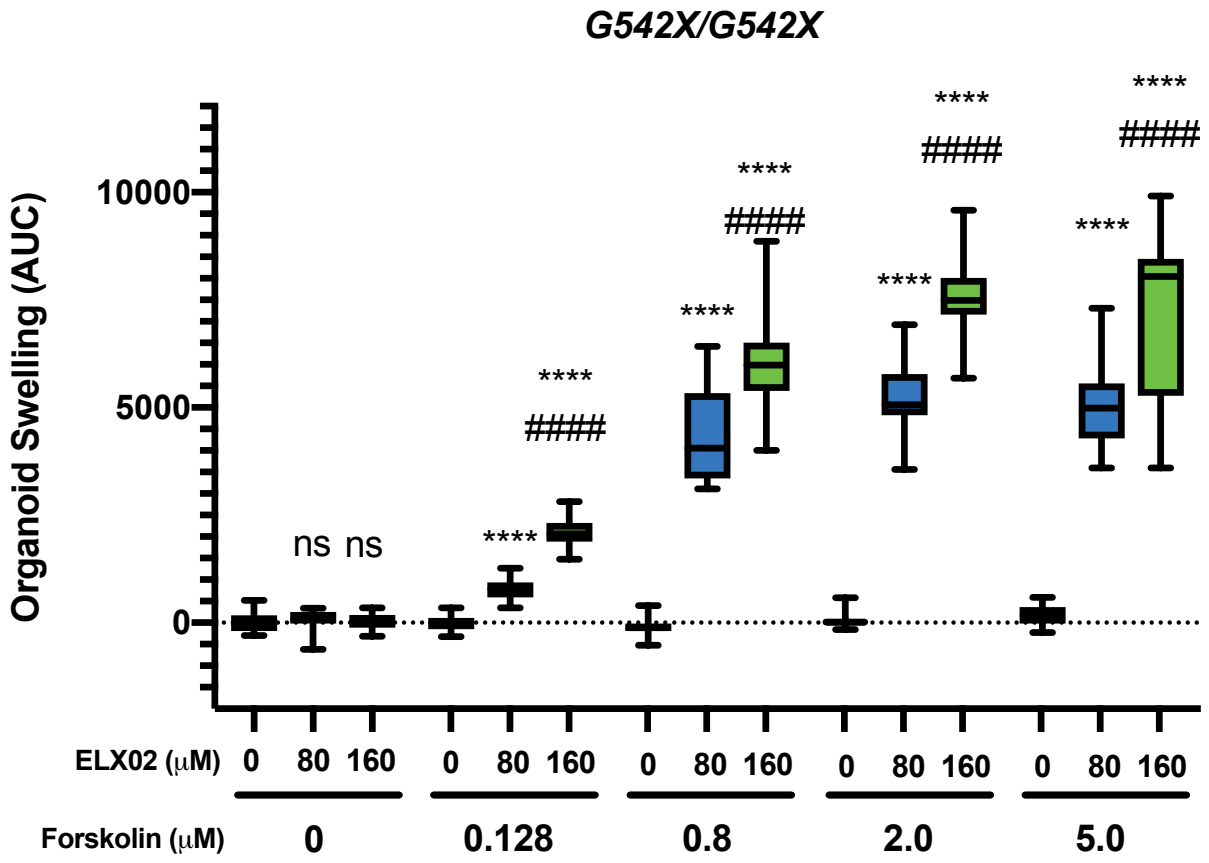
ELX-02 Response in Organoids Compares Favorably to Published Results





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

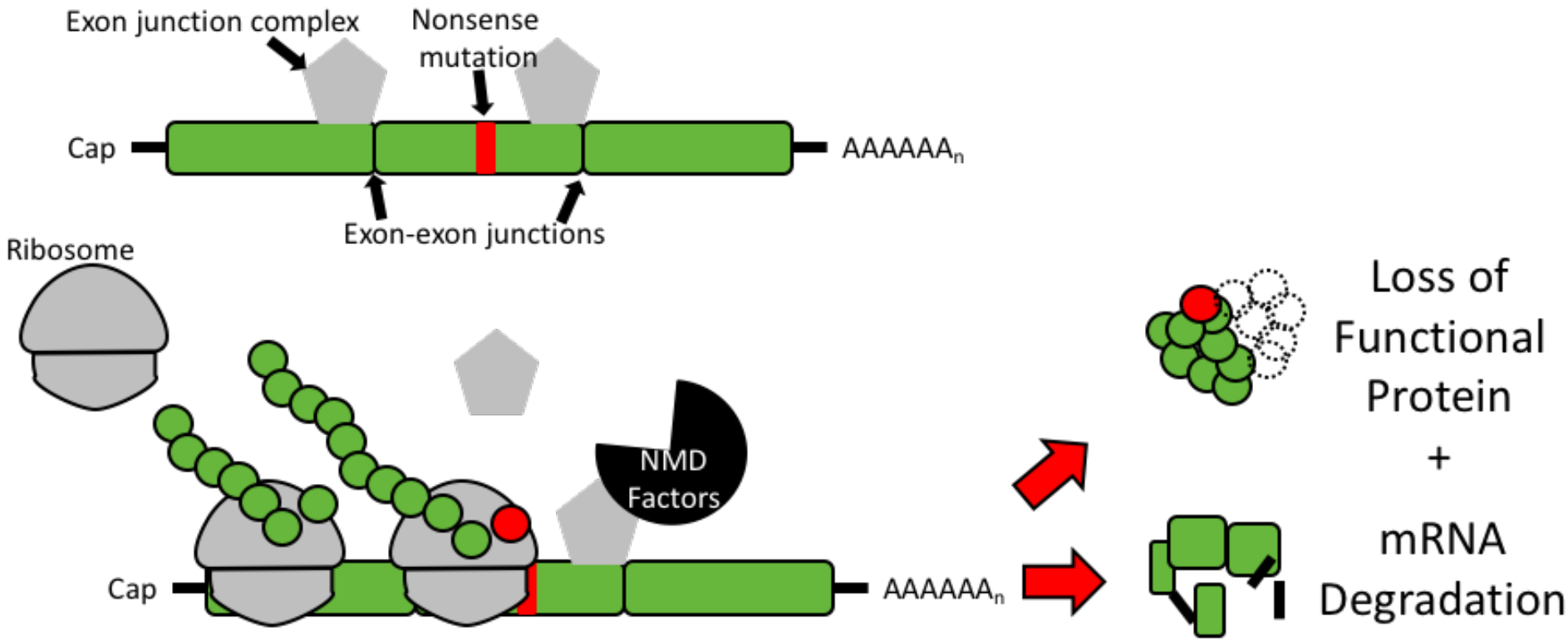
ELX-02 Demonstrates Dose-dependent Read-through Activity to Produce Functional CFTR Protein



- CFTR-dependent organoid swelling is observed across Forskolin induction levels.

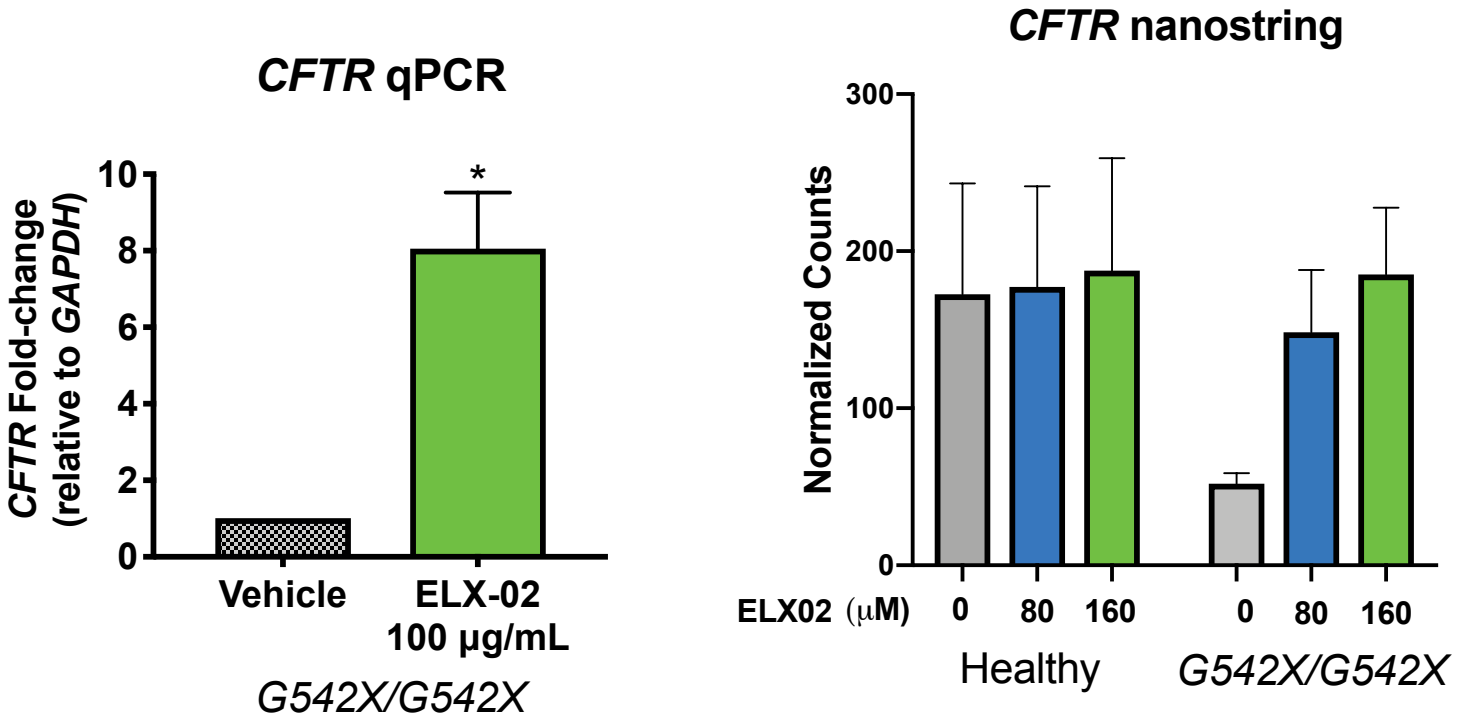
ordinary one-way ANOVA with Tukey's multiple comparison testing was used; ns, non-significant, ***p<0.001 versus vehicle control, **** p<0.0001 versus vehicle control, #### p<0.0001 versus next lower concentration

Nonsense Mutations Often Result in a "Double-hit", Loss of mRNA and Functional Protein



For more information:
Kurosaki & L.E. Maquat. Nonsense-mediated mRNA decay in humans at a glance. J. Cell Sci. 1;129(3):461-7 (2016)

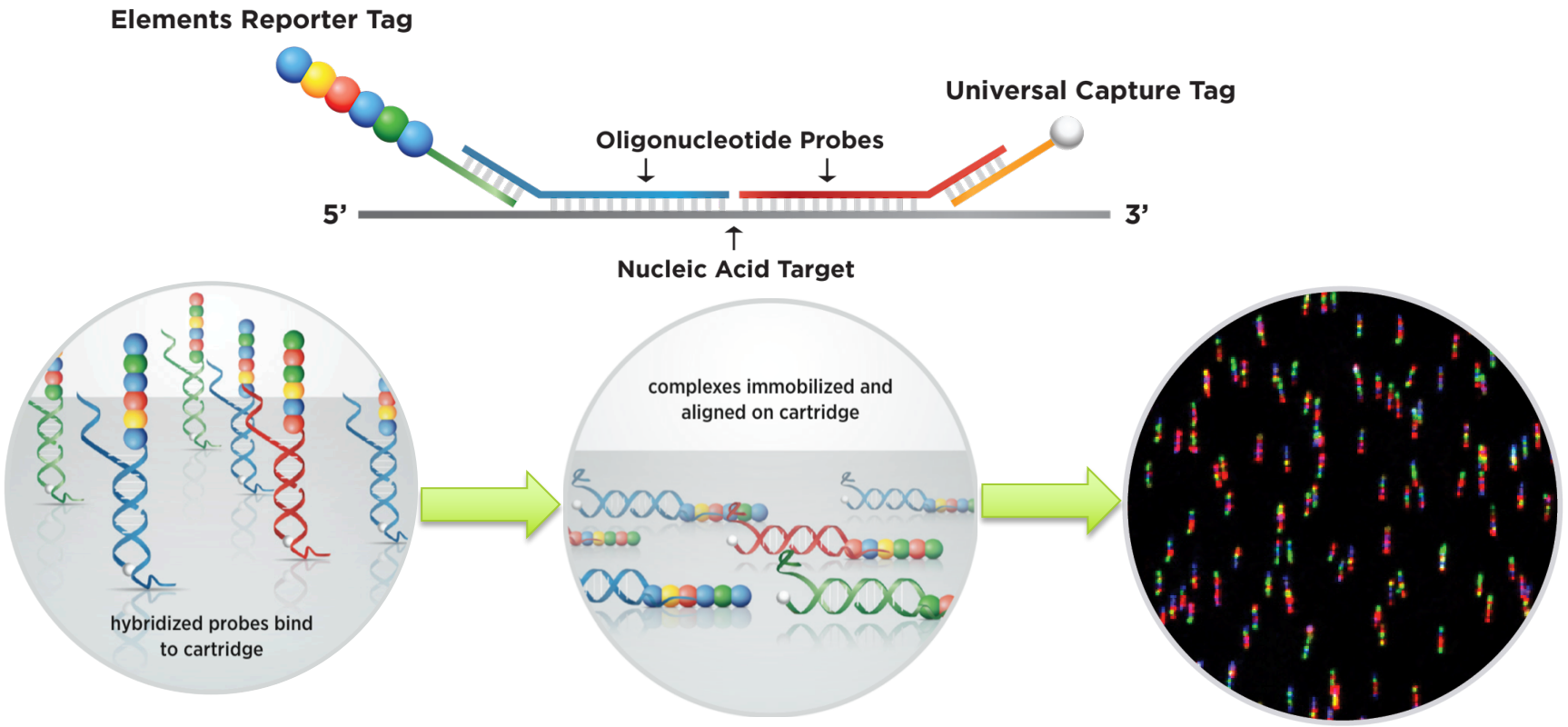
ELX-02 Increases *CFTR* mRNA to Healthy Control Levels

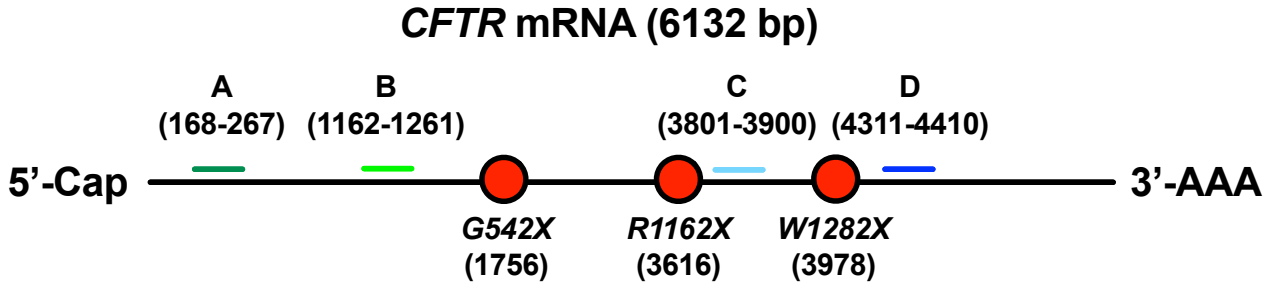


- qPCR primers and Nanostring probe to 3' region of *CFTR* mRNA

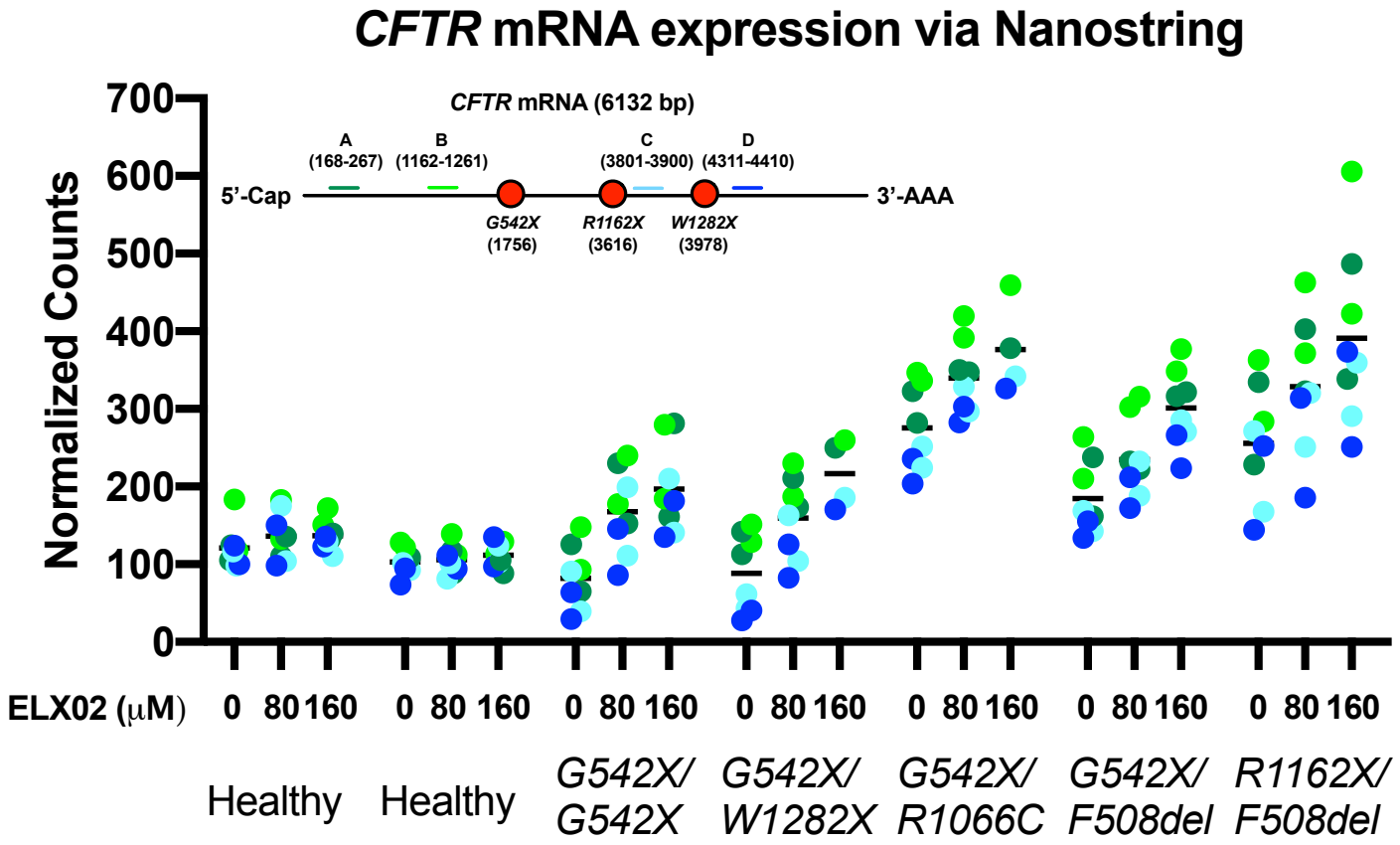
Unpaired t-test, *p<0.05

CFTR Stability Monitoring Using Nanostring





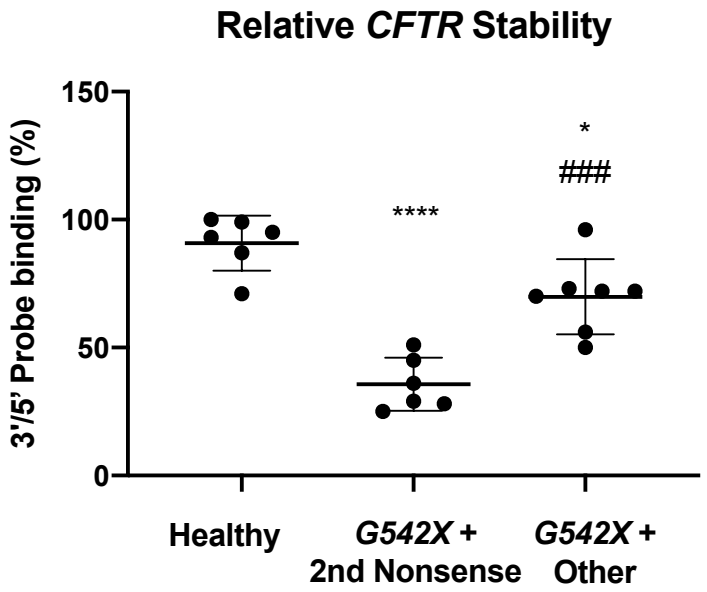
ELX-02 Increases 5′& 3′ *CFTR* mRNA Probe Detection

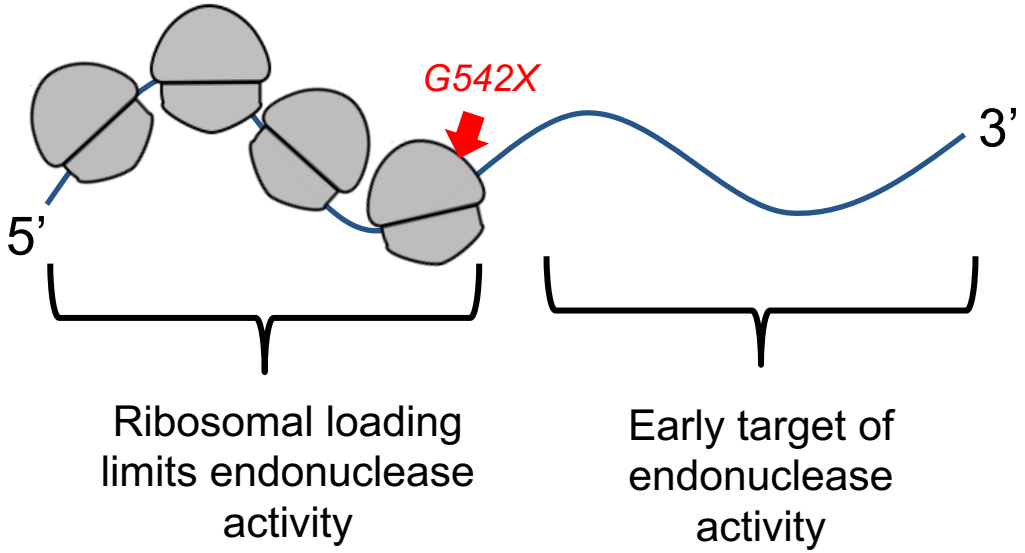


- *CFTR* mRNA varied across genotypes and organoids
  - Consistent with nonsense mediated decay, double nonsense allele organoids had reduced *CFTR* mRNA
- ELX-02 significantly increases in probe detection was observed across all probes in most organoids

Data represent two independent experiments

3′ *CFTR* Probe Binding Is Reduced Relative To 5′ Probes



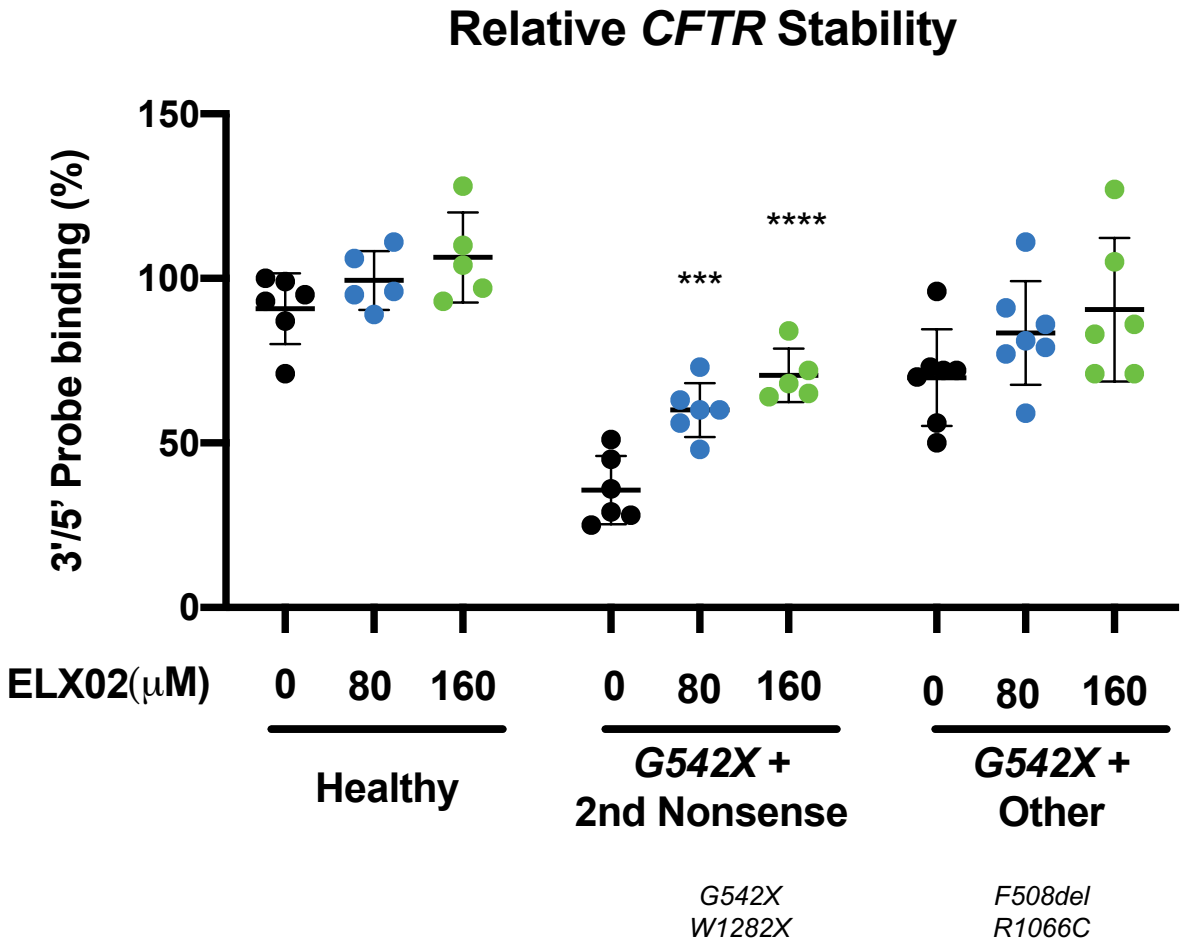


- In healthy (wild-type) organoids 3’ probe detection is 93% of 5’ detection
- In contrast 3’ probe detection is 36% of expected in organoids with two nonsense alleles, 70% in heterozygous nonsense organoids
- Messenger mRNA degeneration may reflect position of nonsense mutation
  - Ribosomes may (temporarily) protect from nonsense mediated decay triggered endonuclease activity.

ordinary one-way ANOVA with Tukey’s multiple comparison testing was used; ns, non-significant, *p<0.05 versus vehicle control, **** p<0.0001 versus vehicle control, ### p<0.001 versus next lower concentration

ELX-02 Increases *CFTR* mRNA Stability in *G542X* Organoids

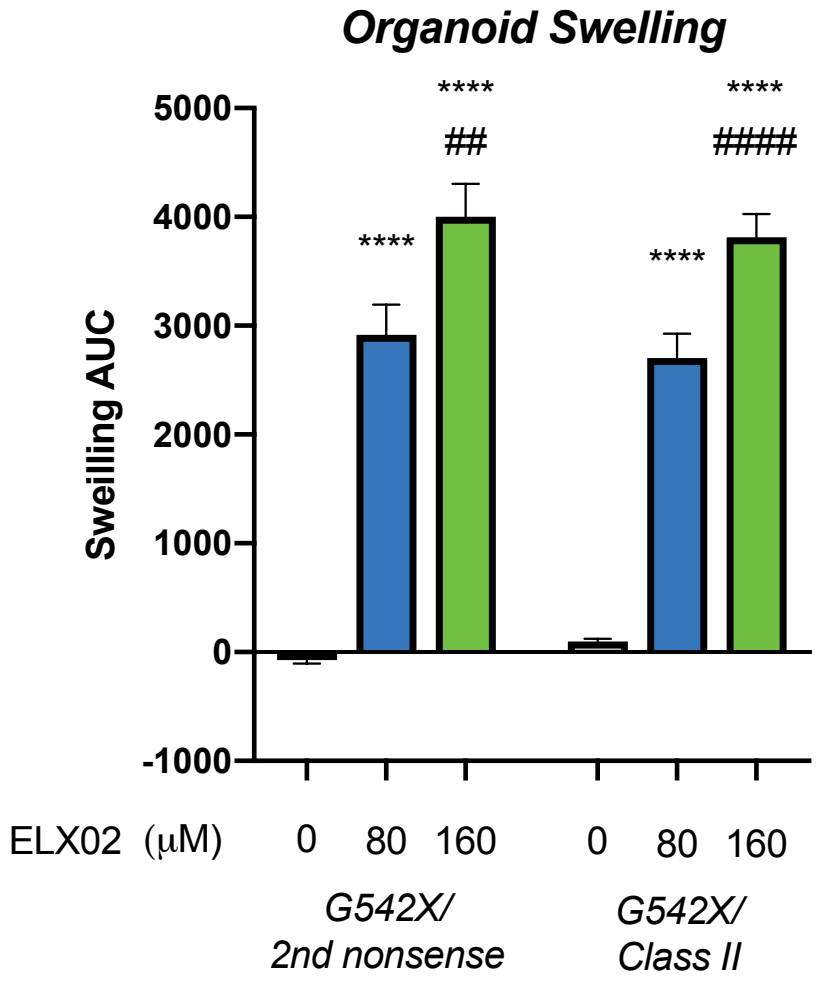
- Relative CFTR stability increases due to ELX-02 are partially attributable to full-length mRNA.
- Organoids bearing two nonsense alleles show significant increases in mRNA stability.
- Effect is also observed in heterozygous organoids.



ordinary one-way ANOVA with Tukey's multiple comparison testing was used; ns, non-significant, ***p<0.001 versus vehicle control, **** p<0.0001 versus vehicle control

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

- Significant increase in organoid swelling is observed in both *G542X* organoids with a second nonsense allele 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 is Progressing to Phase 2 Clinical Studies

- Pronounced CFTR read-through demonstrated in plasmid, HBE, FRT, transgenic mice and patient-derived organoids
- ELX-02 permits dose-dependent increases in *CFTR* mRNA
  - Nonsense mediated decay activity is detectable through 3'/5' binding ratios
- ELX-02 dose-dependently increases *CFTR* mRNA stability
  - Response is most pronounced in organoids bearing two nonsense alleles
  - Contributions of the NMD pathway are currently under evaluation
- ELX-02 increases CFTR function in organoids bearing nonsense alleles representing >75% of the cystic fibrosis nonsense genotype population

Acknowledgements

- Eloxx Cystic Fibrosis Team
- Jasper Mullenders (HUB)

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Thank You