Eloxx Pharmaceuticals

Administration of ELX-02 to Healthy Volunteers Demonstrates Dose-linearity and Proportionality as well as Low Inter-subject Variability

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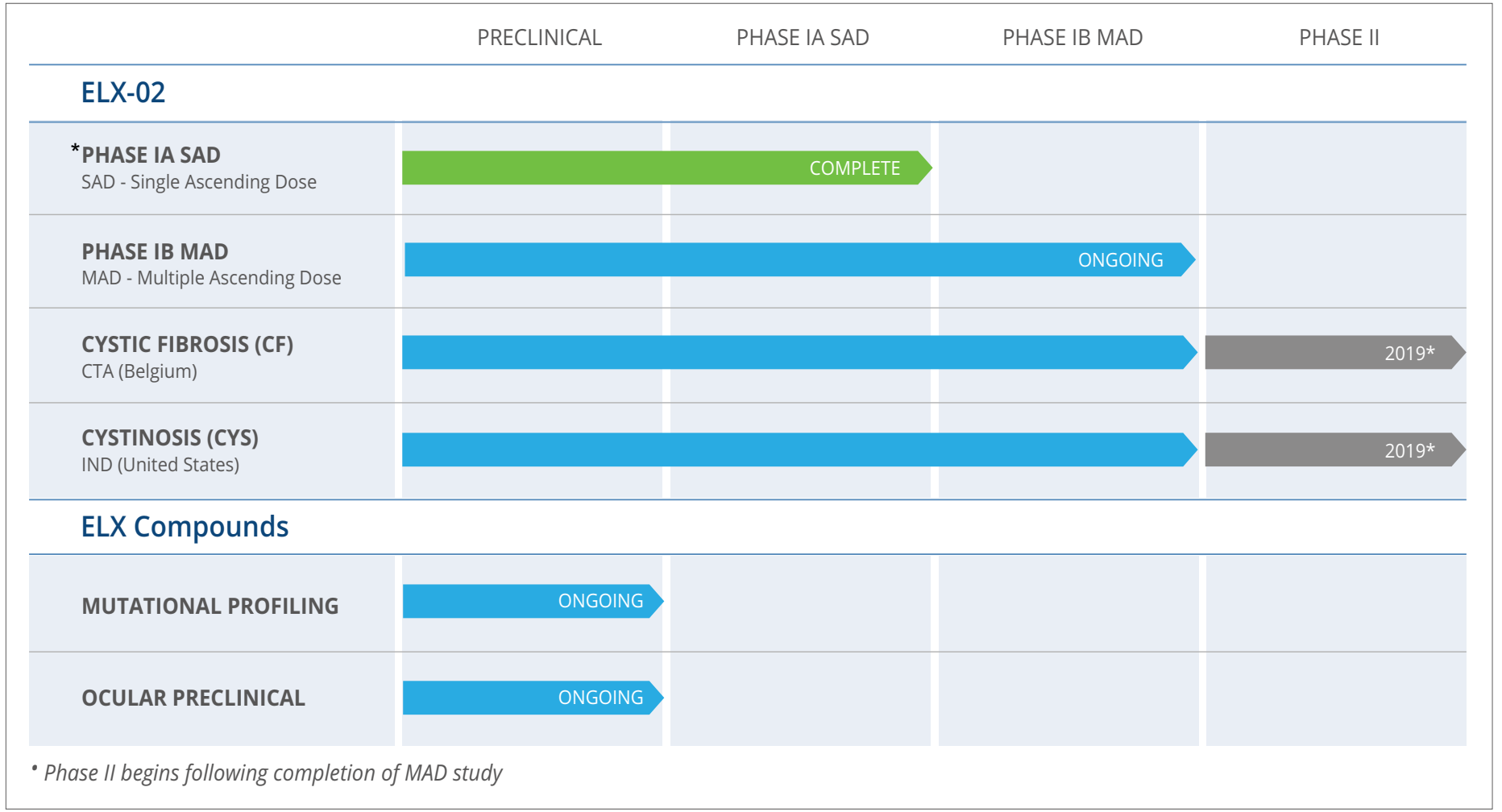
Forward-Looking Statements

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.

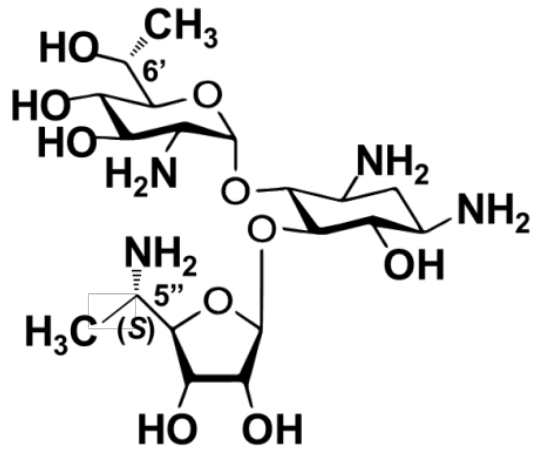
Eloxx Pipeline: Targeting Nonsense Mutation Genotypes for Rare Diseases



*Leubitz A, et. al. Safety, Tolerability, and Pharmacokinetics of Single Ascending Doses of ELX-02, a Potential Treatment for Genetic Disorders Caused by Nonsense Mutations, in Healthy Volunteers. Clin Pharmacol in Drug Dev. 2019 Jan 16. doi: 10.1002/cpdd.647

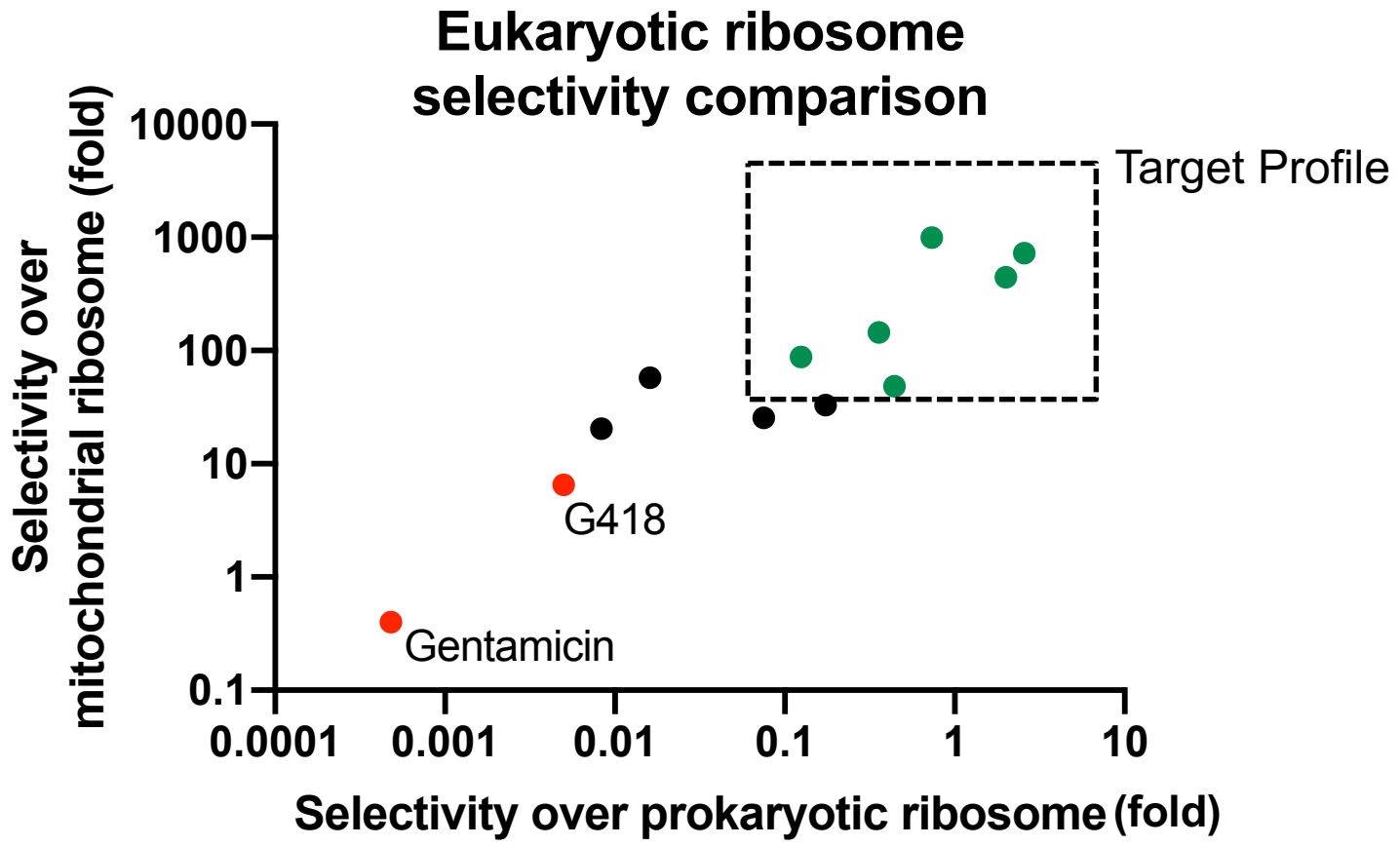
ELX-02: Lead Compound Under Development for Treatment of CF

- Novel small molecule aminoglycoside analogue
  - Classified as an eukaryotic ribosomal selective glycoside (ERSG)
- Designed to have enhanced affinity for eukaryotic ribosomes and a decreased affinity for prokaryotic and mitochondrial ribosomes
- Demonstrates restoration of functional protein production via read-through of premature stop codons caused by nonsense mutations



Physicochemical Properties	
Formula	$C_{19}H_{38}N_4O_{10}\bullet SO_2(OH)_2$
Molecular Weight (sulfate salt)	**580.6 g/mol**
Disassociation Constant	**pKa_1 = 5.74**
Permeability	**low**
Solubility	**> 500 mg/mL in water**

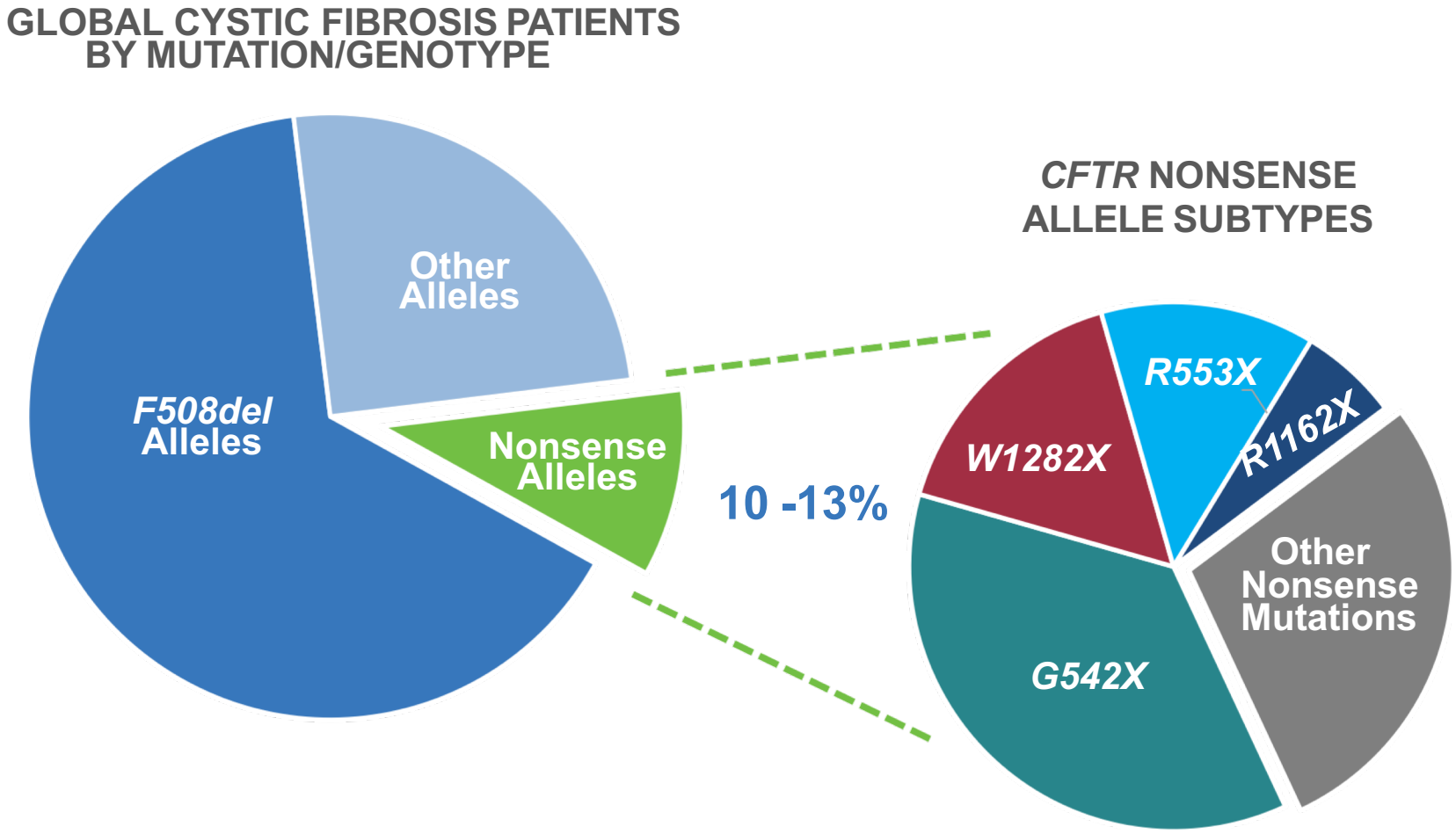
ELX-02 and the Eloxx Library Demonstrate Enhanced Selectivity for Eukaryotic Cytoplasmic Ribosomes to Avoid Off-Target Effects



Data adapted from:
Kandasamy et al. Increased Selectivity toward Cytoplasmic versus Mitochondrial Ribosome Confers Improved Efficiency of Synthetic Aminoglycosides in Fixing Damaged Genes: A Strategy for Treatment of Genetic Diseases Caused by Nonsense Mutations. J. Med. Chem. (2012)

CF Nonsense Mutation Patients – Critical Unmet Needs

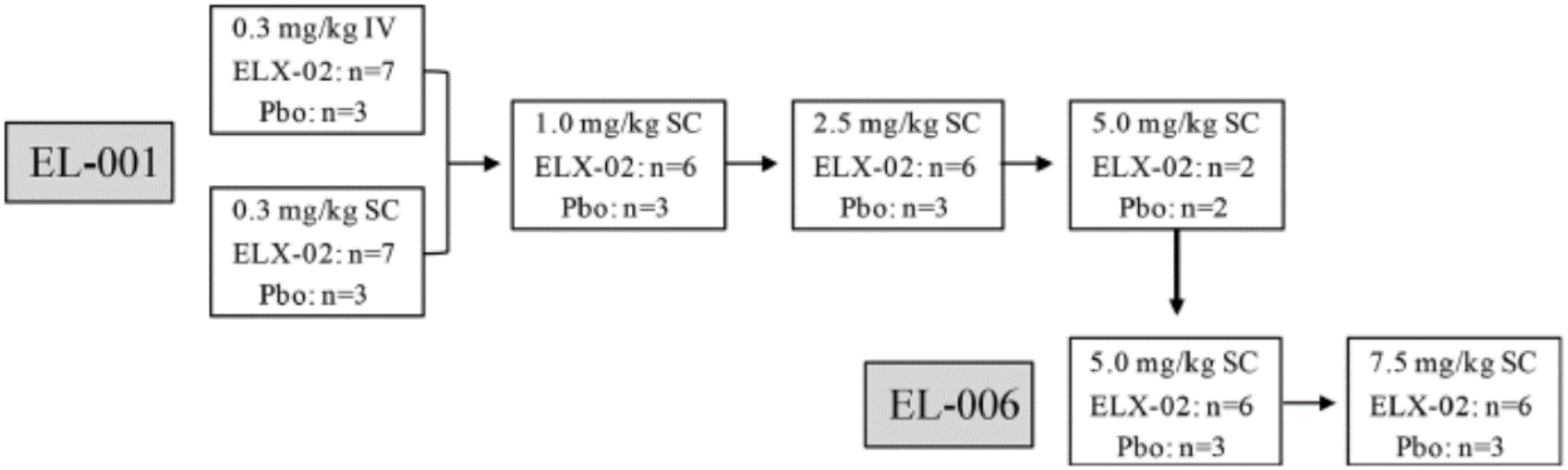
No Currently Approved Drugs To Treat *CFTR* Nonsense Mutations



Source: Eloxx Internal Research/CFTR2 database

Plasma PK from "Single Ascending Dose (SAD) Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of ELX-02 in Healthy Adults*"

- Study Overview/Design
  - 7 cohorts: 5 dose levels (0.3 mg/kg IV&SC, 1.0, 2.5, 5, 7.5 mg/kg SC), Israel and Belgium
  - Randomized (≈ 2:1), double-blind, placebo-controlled, single dose study
  - Visits: Screening (35 days), Dosing day 1, follow up (days 2, 3, 7-11)
  - Dose escalation upon recommendation of a data safety monitoring board



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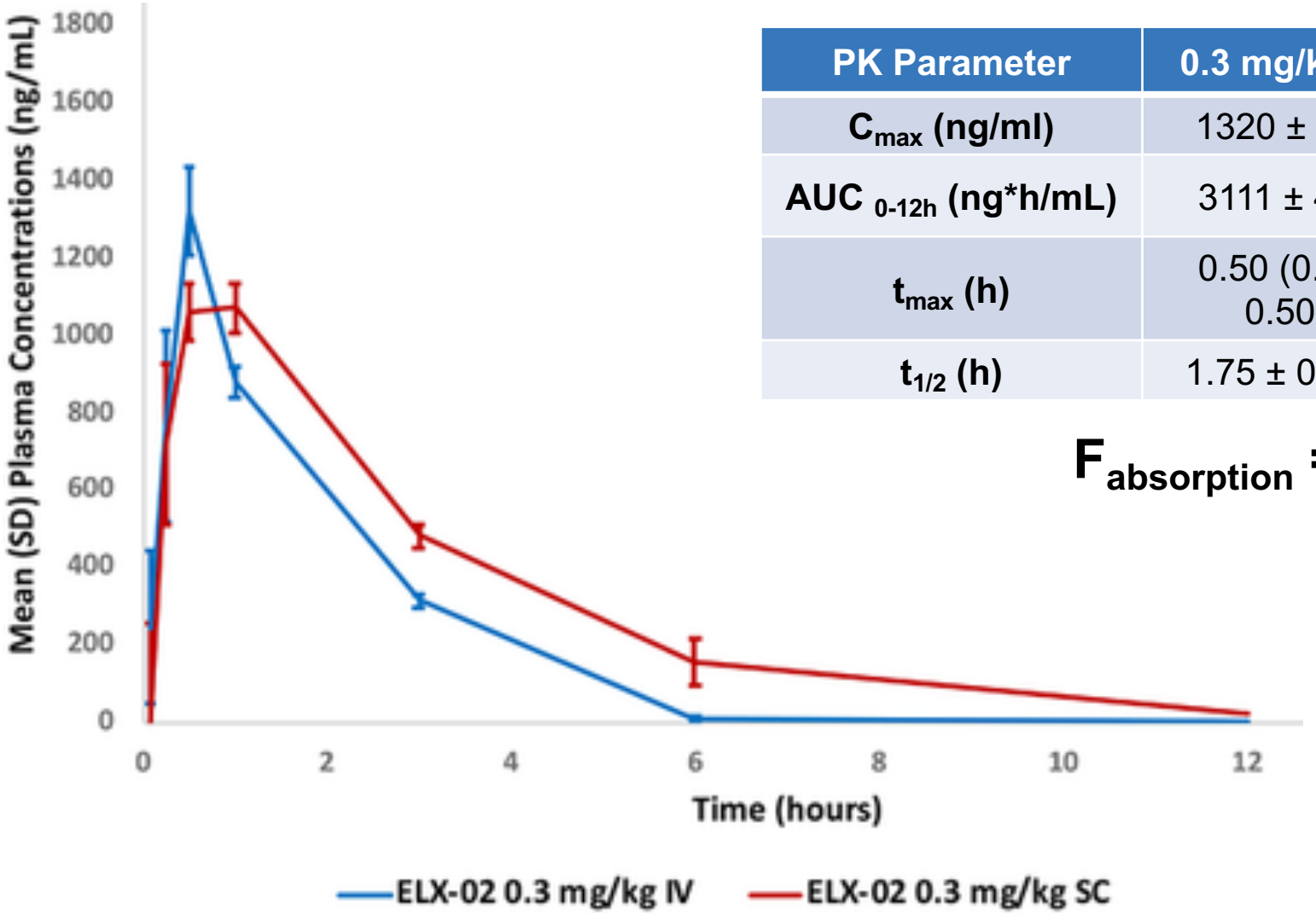
SAD Study Objectives and Safety Evaluations Included …

- Objectives
  - Assess safety and tolerability of single ascending doses
  - Assess plasma and urine pharmacokinetics of SC vs IV administration

- Safety
  - AE's, physical examinations, vital signs, ECG's
  - Auditory assessments
  - Clinical labs (including kidney function)

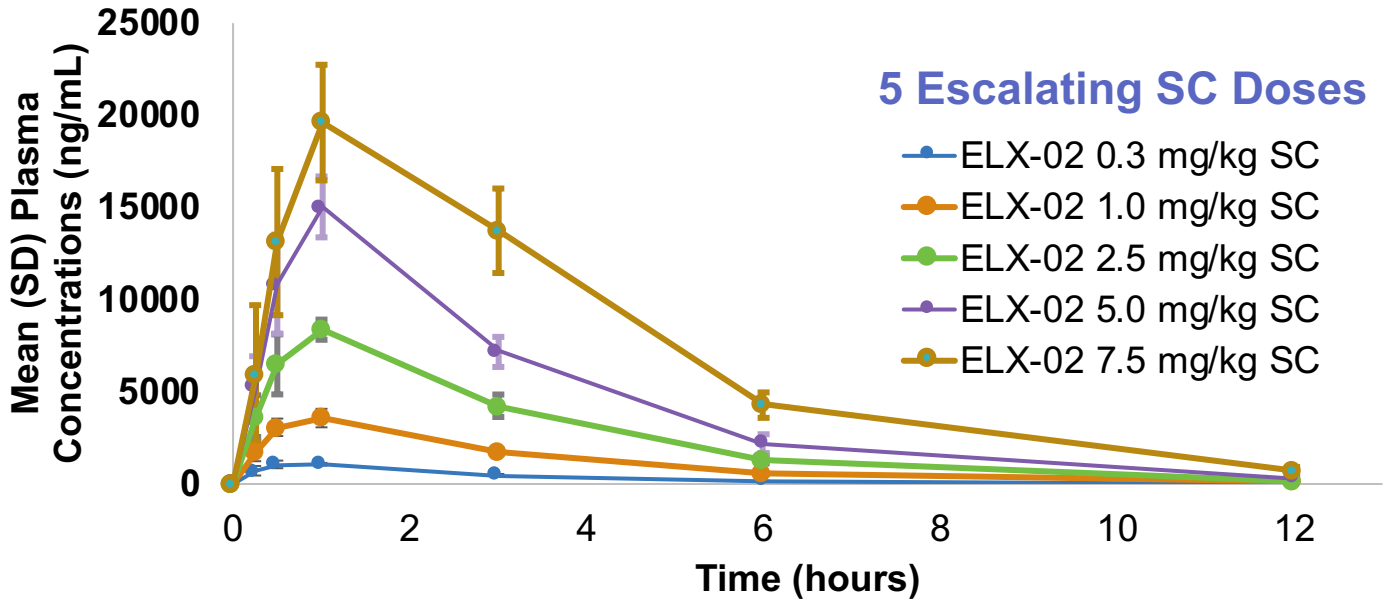
ELX-02 Administered SC is 98% Bioavailable – Plasma PK



PK Parameter	0.3 mg/kg IV	0.3 mg/kg SC
C_{max} (ng/ml)	1320 ± 246	1144 ± 142
AUC $_{0\text{-}12h}$ (ng*h/mL)	3111 ± 413	3891 ± 358
t_{max} (h)	0.50 (0.50-0.50)	0.50 (0.50–1.00)
$t_{1/2}$ (h)	1.75 ± 0.174	2.01 ± 0.155

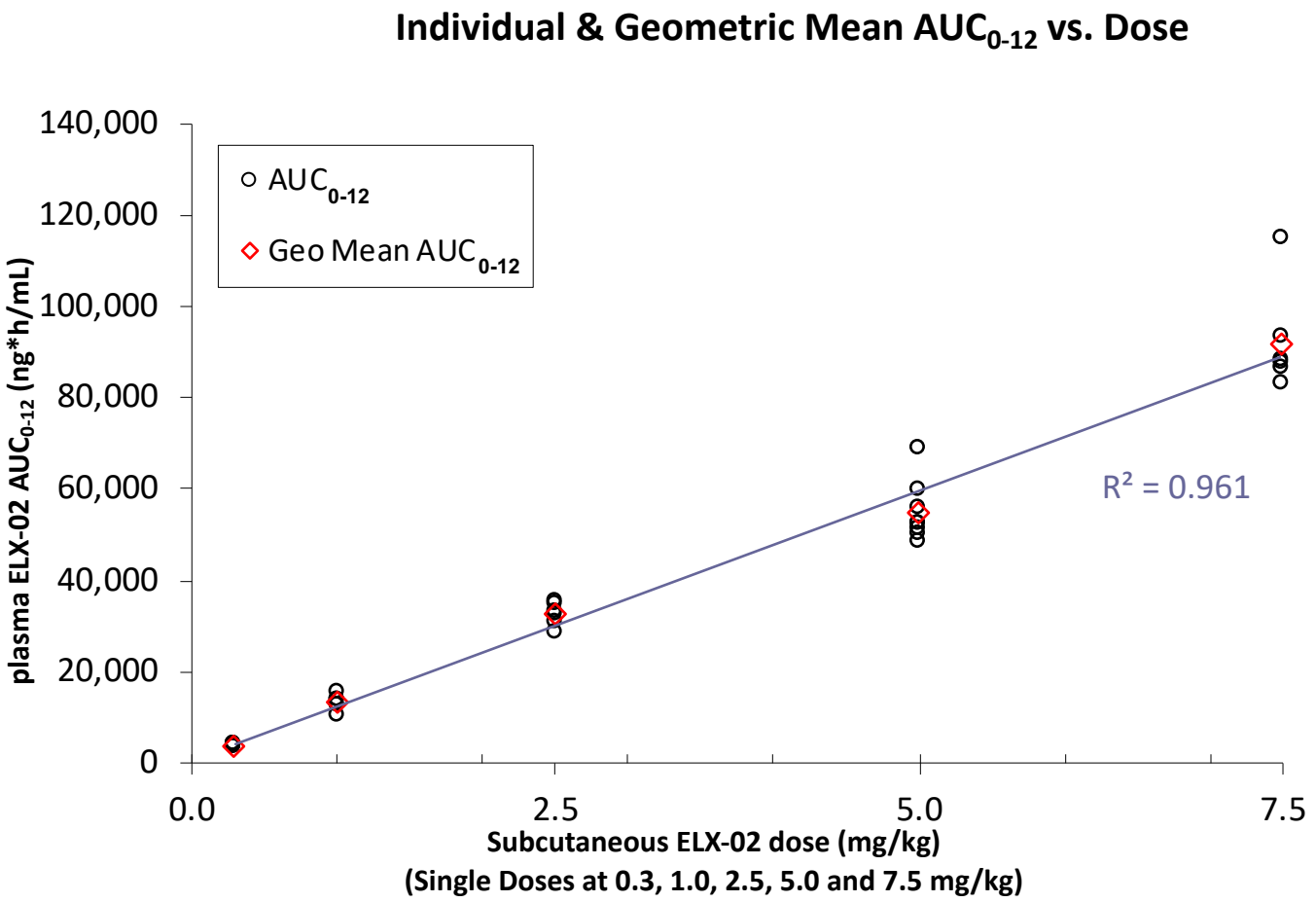
$F_{absorption}$ = 0.98

ELX-02 SC Administration is Dose Proportional – Plasma PK



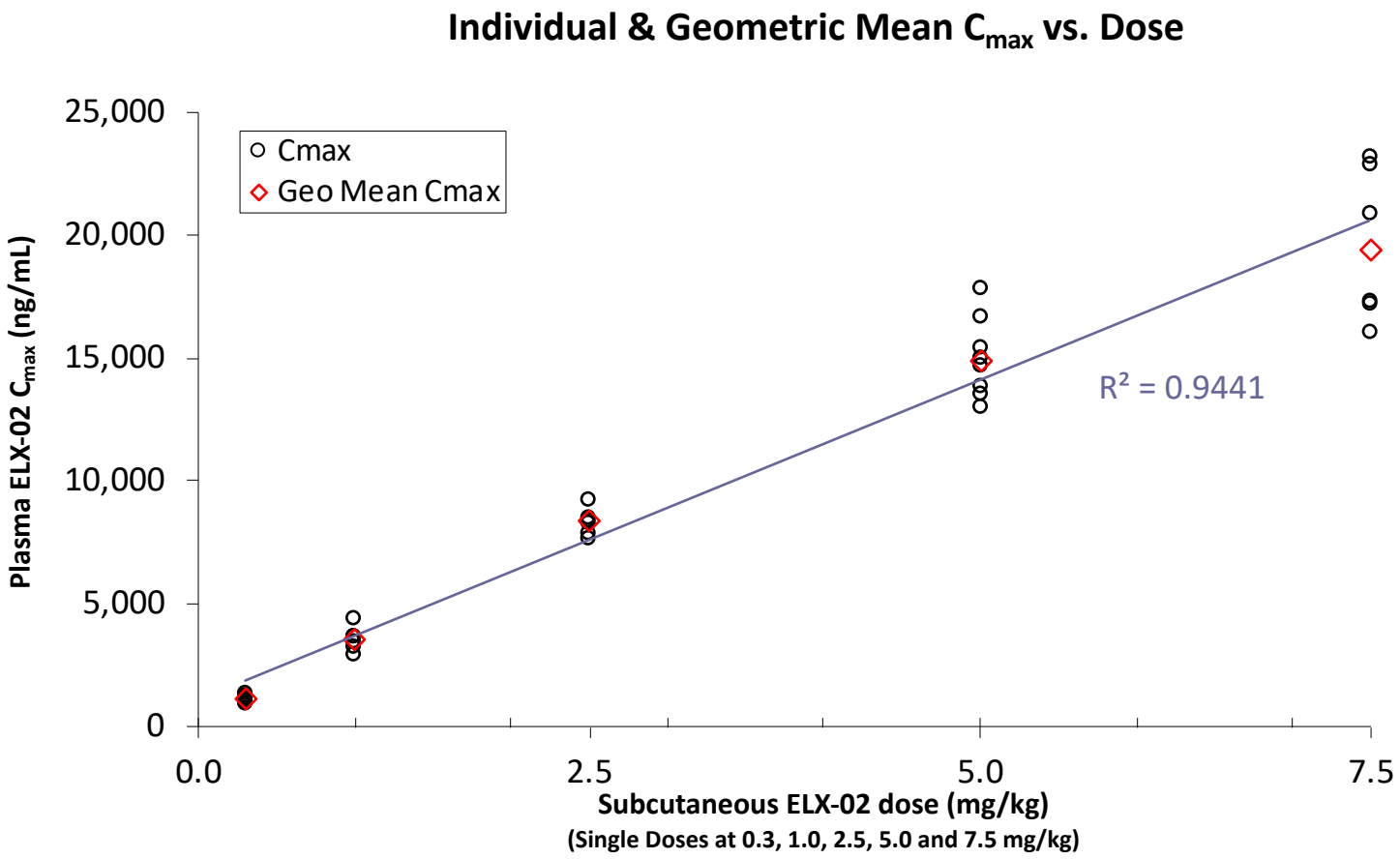
PK Parameter	0.3 mg/kg SC	1.0 mg/kg SC	2.5 mg/kg SC	5.0 mg/kg SC	7.5 mg/kg SC
C_{max} (ng/ml)	1144 ± 142	3576 ± 502	8370 ± 548	15,030 ± 1652	19,605 ± 3137
C_{max} CV%	12.4	14.0	6.54	11.0	16.0
AUC $_{0\text{-}12h}$ (ng*h/mL)	3891 ± 358	13,131 ± 1729	31,153 ± 2380	52,946 ± 6074	86,891 ± 10,439
AUC CV%	9.19	13.2	7.64	11.5	12.0
t_{max} (h)	0.50 (0.50–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (1.00–1.00)
$t_{1/2}$ (h)	2.01 ± 0.155	2.14 ± 0.373	2.86 ± 0.178	3.73 ± 1.08	8.11 ± 3.19

ELX-02 SC Plasma PK Shows AUC Linearity & Dose Proportionality



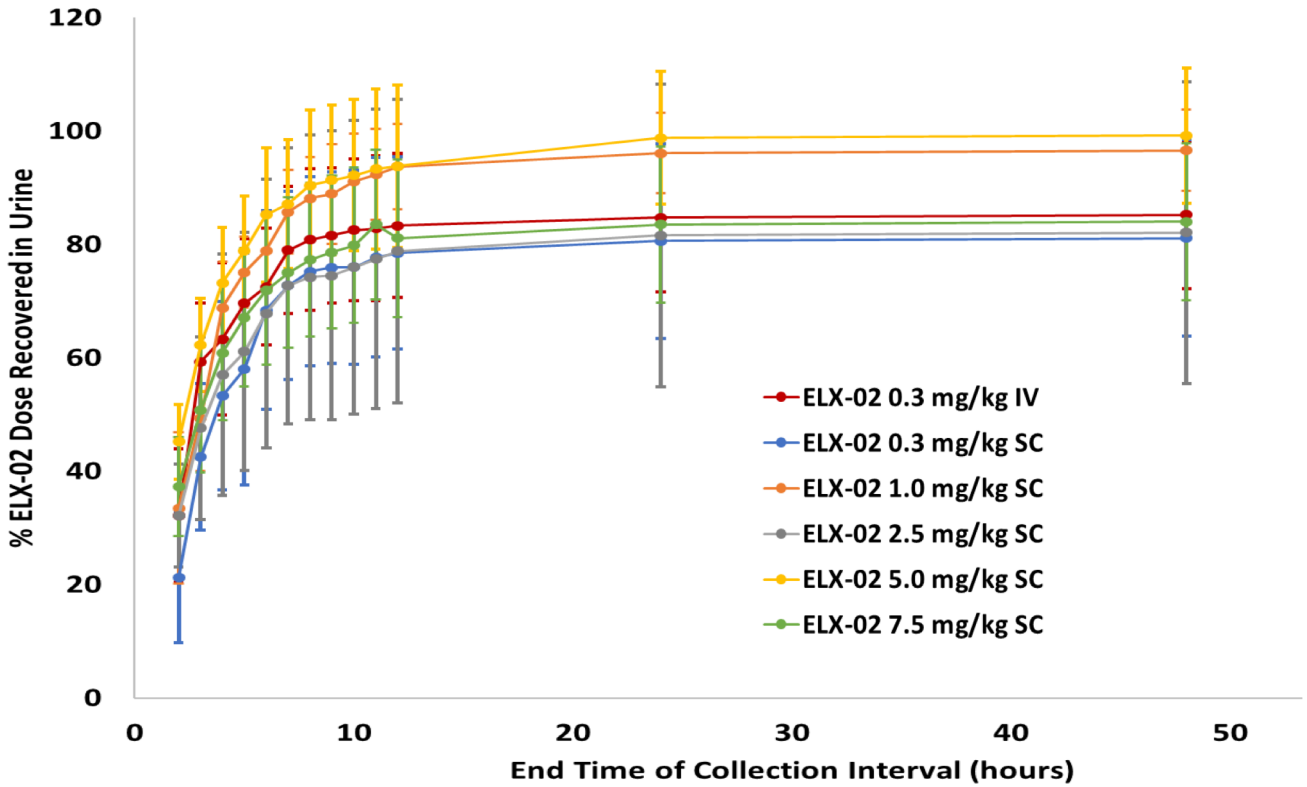
- AUC shows linearity and dose proportionality (24-fold increase for a 25-fold dose increase) across all dose levels

ELX-02 SC Plasma PK Shows C_{max} Linearity & Dose Proportionality



- Cmax shows linearity and dose proportionality (17-fold increase for a 25-fold dose increase) across all dose levels

Primary Route of ELX-02 Elimination is Renal as Parent Molecule – Recovery in Urine



Result	0.3 mg/kg IV	0.3 mg/kg SC	1.0 mg/kg SC	2.5 mg/kg SC	5.0 mg/kg SC	7.5 mg/kg SC
$Ae_{0\text{-}12h}$ (%dose excreted)	83.3 ± 12.7	78.5 ± 17.0	93.7 ± 7.47	78.8 ± 26.8	93.8 ± 14.3	81.1 ± 13.9
$Ae_{12\text{-}24h}$ (%dose excreted)	84.7 ± 13.1	80.6 ± 17.2	96.1 ± 7.06	81.6 ± 26.7	98.8 ± 11.7	83.5 ± 13.8
$Ae_{24\text{-}28h}$ (%dose excreted)	85.2 ± 13.0	81.1 ± 17.3	96.6 ± 7.14	82.1 ± 26.6	99.2 ± 11.9	84.0 ± 13.8

ELX-02 Was Generally Well Tolerated

- No Serious Adverse Events (SAEs)
- All AEs mild in severity
- No nephrotoxicity or ototoxicity
- Subjects with at least 1 TEAE:
  - ELX-02 25/40 (62.5%)
  - Placebo 9/20 (45.0%)
- The most frequent AEs considered ELX-02 related:
  - Pooled injection site events 11/40 (27.5%)
  - 2/20 (10%) in placebo
- Additional AEs included headache, ear discomfort, and dizziness

Original Manuscript

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Safety, Tolerability, and Pharmacokinetics of Single Ascending Doses of ELX-02, a Potential Treatment for Genetic Disorders Caused by Nonsense Mutations, in Healthy Volunteers

Clinical Pharmacology in Drug Development
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Abstract

ELX-02 is an investigational synthetic eukaryotic ribosome–selective glycoside optimized as a translational read-through molecule that induces read through of nonsense mutations, resulting in normally localized full-length functional proteins. ELX-02 is being developed as a therapy for genetic diseases caused by nonsense mutations. Two phase 1a, randomized, double-blind placebo-controlled, single-ascending-dose studies were conducted in healthy human subjects to evaluate the safety and pharmacokinetics of ELX-02. Single subcutaneously injected doses of ELX-02 between 0.3 mg/kg and 7.5 mg/kg showed an acceptable safety profile without severe or serious drug-related adverse events, including a lack of renal and ototoxicity events. Injection of ELX-02 resulted in a rapid time to peak concentration and elimination phase, with complete elimination from the vascular compartment within 10 hours. ELX-02 area under the concentration-time curve to infinity showed dose-exposure linearity (24-fold increase for a 25-fold dose increase), and the maximum concentration showed dose proportionality (17-fold increase for a 25-fold increase). The mean apparent volume of distribution was dose dependent, suggesting an increased distribution and tissue uptake of ELX-02 at higher doses. The primary route of excretion was in the urine, with the majority of the compound excreted unchanged. These results support the evaluation of the safety, pharmacokinetics, and efficacy of repeat dosing in future studies.

Keywords

ELX-02, safety, pharmacokinetics, single ascending dose, phase 1, healthy volunteers, genetic disorders, nonsense mutations, aminoglycoside, translational readthrough

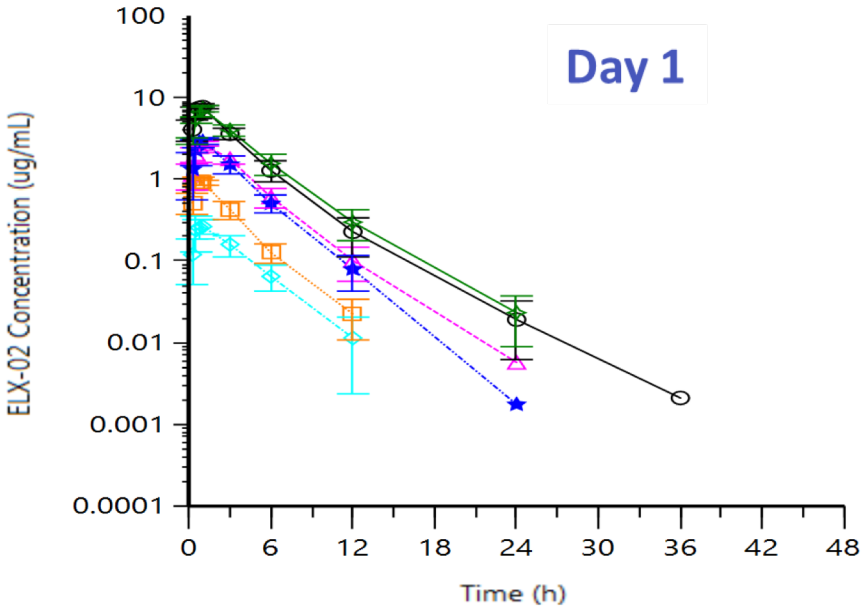
Leubitz A, et. al. Safety, Tolerability, and Pharmacokinetics of Single Ascending Doses of ELX-02, a Potential Treatment for Genetic Disorders Caused by Nonsense Mutations, in Healthy Volunteers. Clin Pharmacol in Drug Dev. 2019 Jan 16. doi: 10.1002/cpdd.647

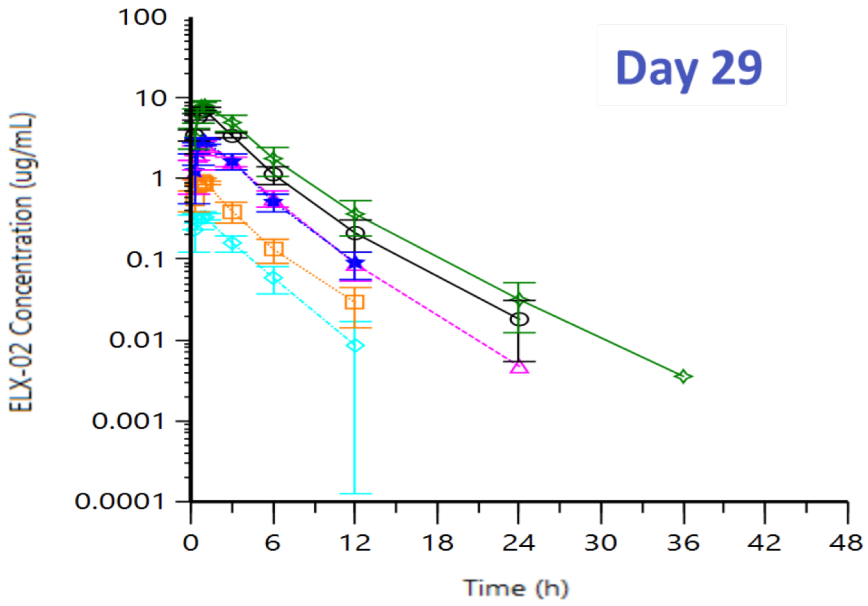
Plasma PK from "Multiple Ascending Dose (MAD) Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of ELX-02 in Healthy Adults"

Preliminary Results from Ongoing Study

6 Cohorts to Date (b.i.w.)

- COHORT 1 (0.1 mg/kg b.i.w.)
- COHORT 2 (0.3 mg/kg b.i.w.)
- COHORT 3 (1.0 mg/kg b.i.w.)
- COHORT 4 (2.5 mg/kg b.i.w.)
- COHORT 5 (1.0 mg/kg b.i.w.)
- COHORT 6 (2.5 mg/kg b.i.w.)





- AUC and C_{max} are similar to those observed in the single dose trial
- Dose proportional exposures and lack of accumulation up to day 29
- T_{max} 0.75-1.17 hr (MAD) vs 0.5-1.0 hr (SAD)
- Mean $t_{1/2}$ 2.06-3.10 hr (MAD) vs 2.01-8.11 hr (SAD)

Summary and Conclusions

- ELX-02 has been generally well tolerated in clinical studies to date, supporting future evaluation in Phase 2 with patients having nonsense mediated CF
- ELX-02 shows high bioavailability (98%) upon subcutaneous administration with highly reproducible pharmacokinetics
- ELX-02 administered SC shows linear and dose proportional $AUC_{0\text{-}12}$ and C_{max} over the dosage range studied (0.3 to 7.5 mg/kg)
- Consistent results were observed across single and multiple dose studies, with no accumulation
- Elimination is primarily renal as parent compound

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Thank You