Clinical Stage Neurology Company Focused on Neuronal Excitability Disorders

Corporate Presentation | May 2023

eliem Therapeutics

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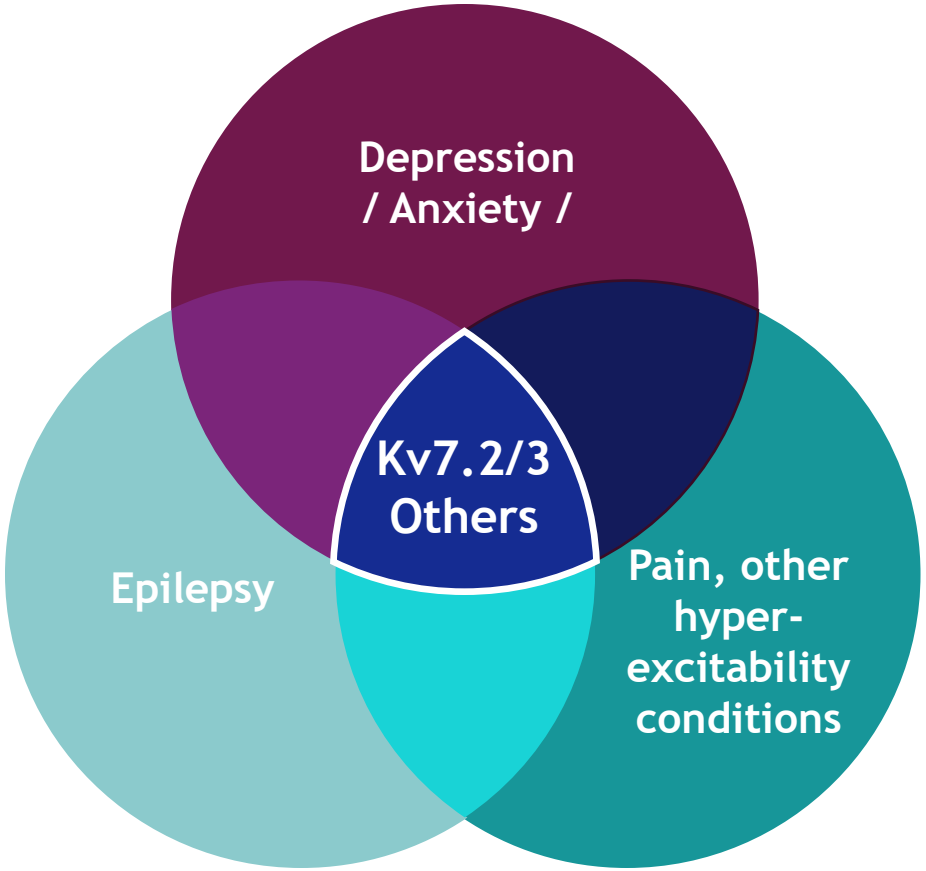
Rethinking treatment for nervous system disorders

- **Highly experienced** team with deep expertise in neuroscience and ion channel drug discovery and development
- **Highly differentiated Kv7 program** with broad potential to pursue across multiple neuronal excitability indications
- **~$109M* cash runway into 2027** enabling advancement of lead Kv7 asset through Phase 2a clinical proof of concept

* cash, cash equivalents and investments as of March 31, 2023

Addressing multiple interrelated diseases by focusing on core mechanisms of neuronal excitability



Approaching **interrelated disease states** with distinct MOAs

Innovating within **clinically validated** mechanisms of action

Pursuing products with **multiple potential indications**

Eliem Portfolio: Focused on clinically validated Kv7.2/3 mechanism with potential to pursue across multiple neuronal excitability disorders

Product Candidate (Mechanism)	Potential Indications	Lead selection / optimization	IND-enabling studies	Phase 1	Phase 2	Phase 3
ETX-123 (Kv7.2/3 channel opener)	• Epilepsy • Depressive disorders • Chronic Pain • Other CNS hyperexcitability disorders			Phase 1 in healthy subjects planned for 1H 2024 initiation		
Backup Kv7.2/3 openers						
ETX-155* (GABAA PAM neurosteroid)	• Depression / Anxiety • Epilepsy			(On hold as of Feb 2023)		

* ETX-155 (GABAA positive allosteric modulator) is a Phase 2-ready asset in Eliem's portfolio but development has been paused as of Feb 2023

Kv7 Opener

Lead candidate ETX-123 selected
Phase 1 planned 1H 2024

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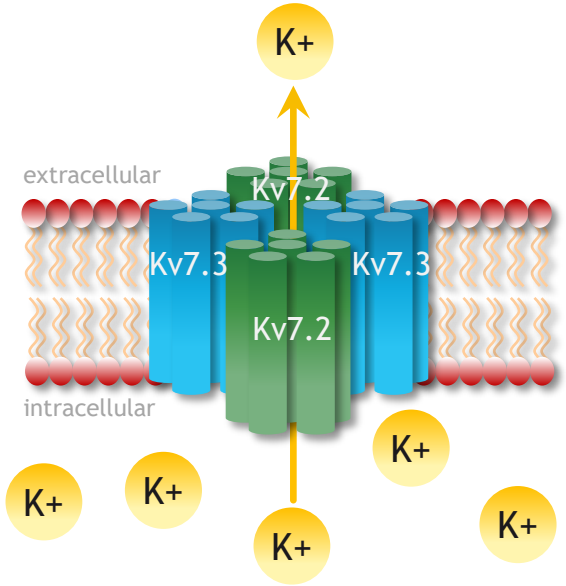
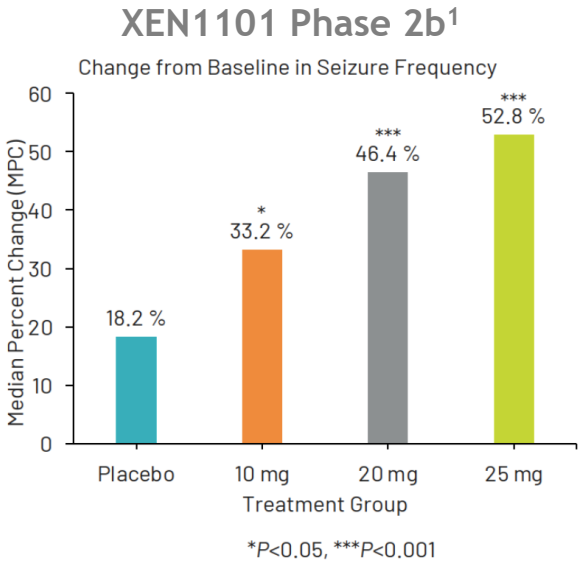
Kv7.2/3 potassium channel: a clinically validated regulator of neuronal hyperexcitability with significant commercial potential

Core mechanism to regulate hyperexcitability



*Kv7.2/Kv7.3 heteromers mediate **the neuronal M-current, widely regulating neuronal excitability** by enabling the outflow of potassium ions, to dial down action potential firing*

Highly compelling efficacy for Kv7.2/3 MOA in refractory epilepsy



Broad potential for expansion into numerous CNS hyperexcitability indications

Commercial potential reflected in valuations for clinical stage Kv7 programs

Company	Asset	Stage	Mkt Cap[2]
Xenon (XENE)	XEN1101	Ph 3	~$2.6b
Biohaven (BHVN)	BHV-7000	Ph 1	~$921m

*BHVN acquired BHV-7000 program for **$1.24b ($100M upfront)** at preclinical stage in Feb 2022*

[1] French et al, AES Annual Meeting 2022
[2] Est. market cap as of May 4, 2023

Kv7.2/3 Program: Developing a differentiated Kv7.2/3 opener for multiple neuronal excitability indications

Kv7 Opportunity

Strong clinical validation in pain and epilepsy
(retigabine, flupirtine, XEN1101)

Human genetic validation

Metabolic safety liabilities with existing molecules and opportunity to improve tolerability

Clear translational path to clinical efficacy

Eliem Kv7 Program Objectives

Identify novel Kv7 openers with:

- Potent activity at Kv7.2/3
- Better selectivity over other Kv7 subtypes (Kv7.4 / 7.1)
- Improved metabolic stability
- Reduced off-target activity (GABA, other ion channels)
- Improved safety and tolerability

Program Status

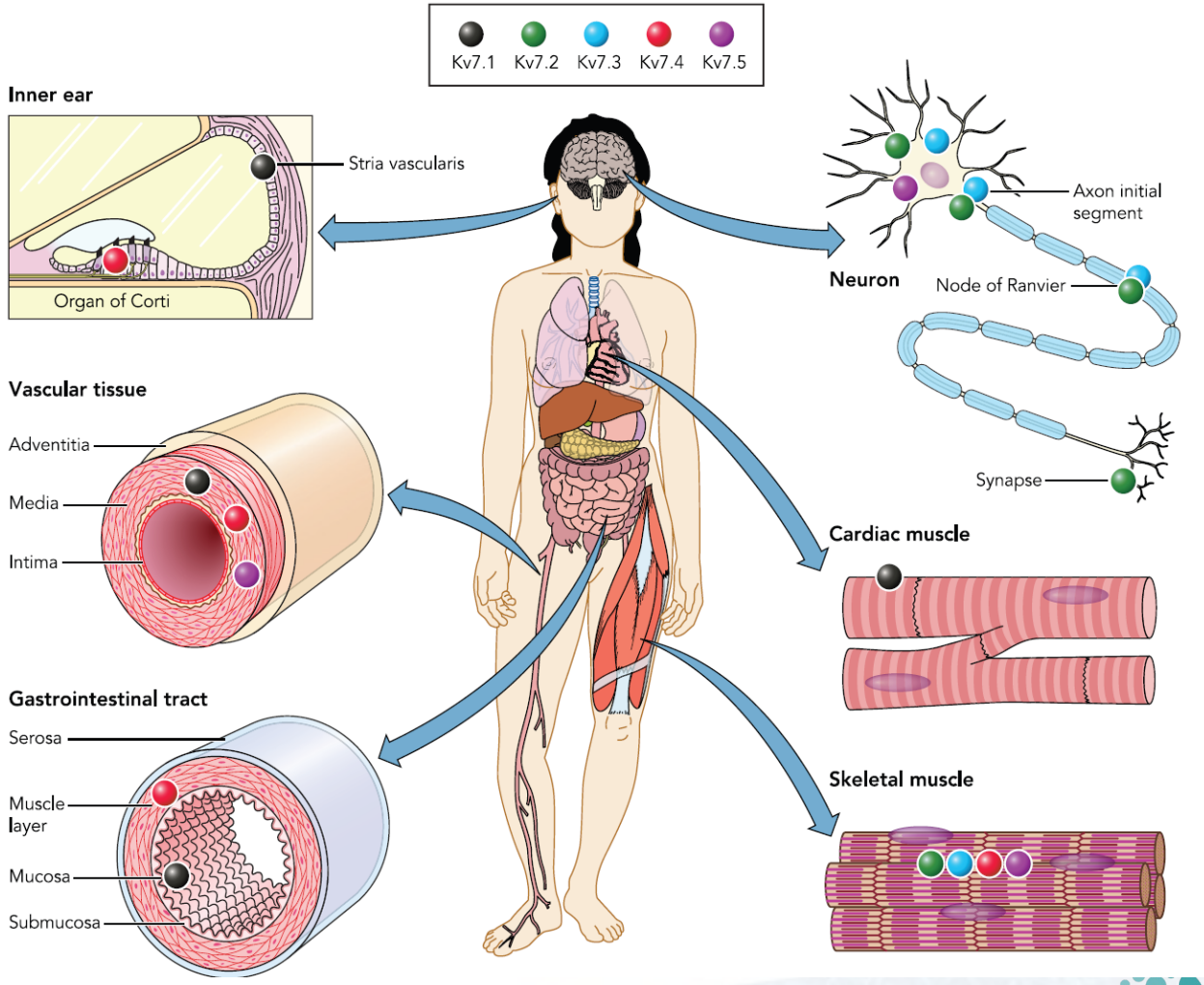
Foundational IP filed in novel chemical space distinct from known Kv7 openers

Lead candidate ETX-123 selected, progressing into Phase 1 in 1H 2024

Kv7 channels provide a convergent mechanism to control hyperexcitability in CNS, PNS, and other tissues

- The Kv7 family consists of 5 different subtypes with different electrophysiological properties and tissue expression:
  - **Kv7.1:** cardiac tissue
  - **Kv7.2 and Kv7.3:** CNS and PNS (all brain resident cells)
  - **Kv7.4:** smooth muscles, cardiac mitochondria, and inner ear
  - **Kv7.5:** CNS, smooth and skeletal muscles

Loss of function mutation of KCNQ2 and 3 (genes encoding for Kv7.2 and 7.3) have been associated with the onset of epilepsy syndromes and encephalopathies

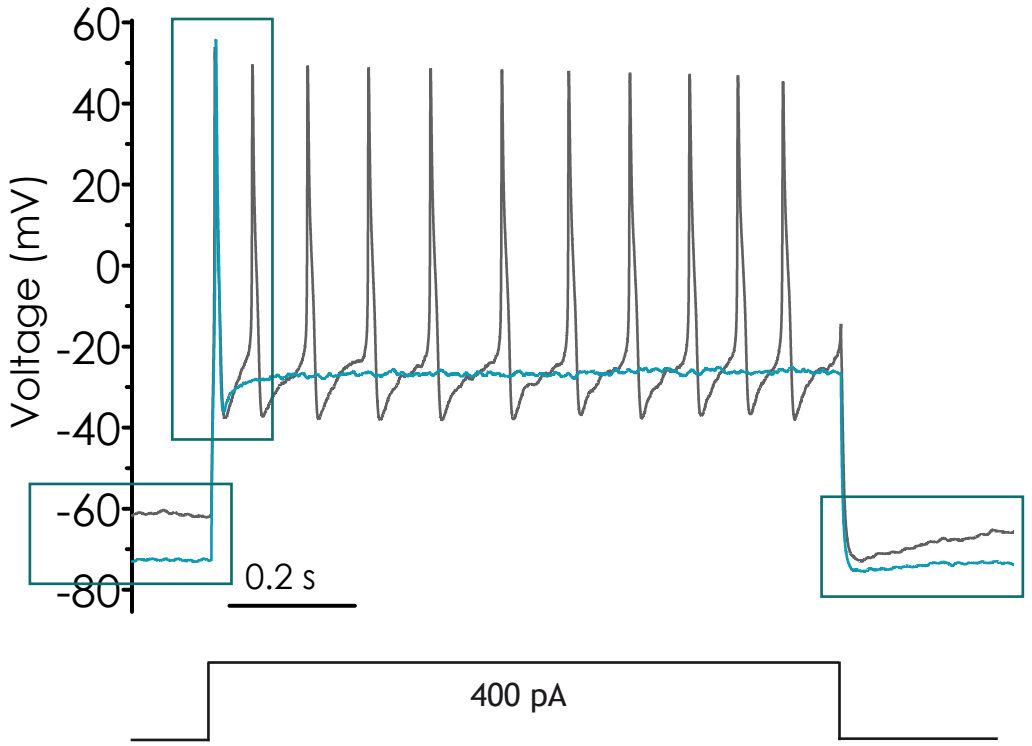


Source: Soldovieri et al., 2011

Mechanism: Kv7.2/3 openers decrease neuronal excitability by hyperpolarizing the membrane potential and reducing of action potential firing in excitable cells

Decrease of action potential firing

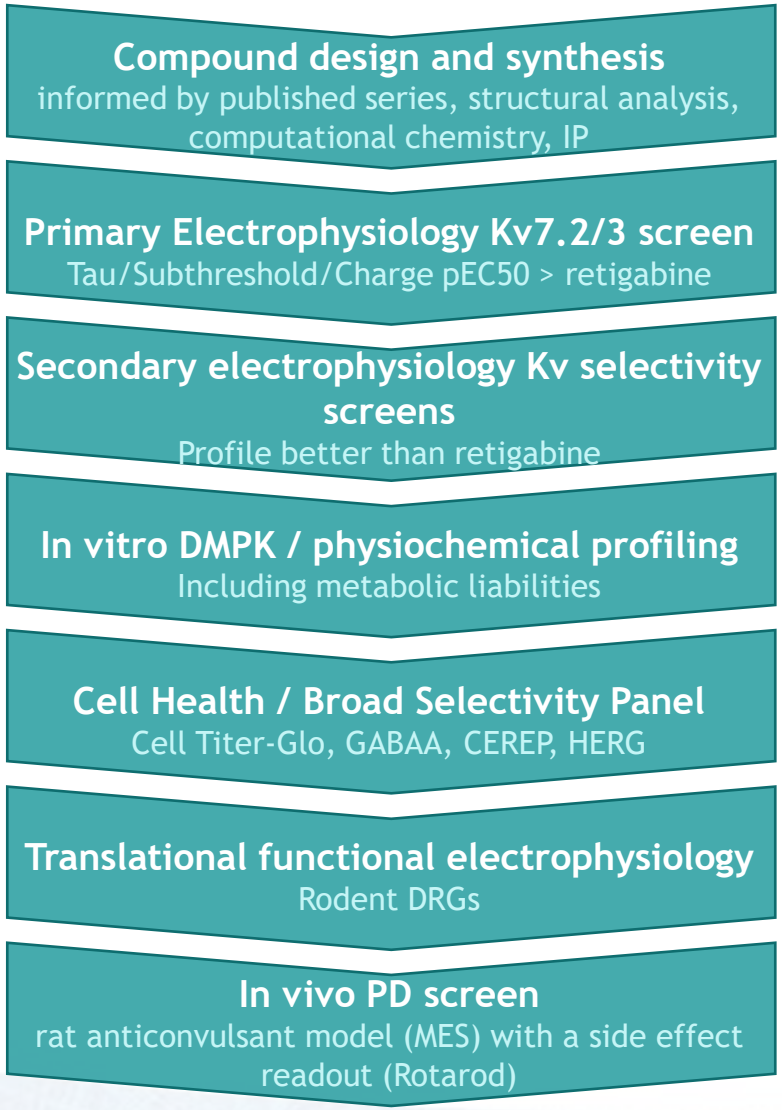
Hyperpolarization and decrease of resting membrane potential



Baseline
Kv7 channel activator

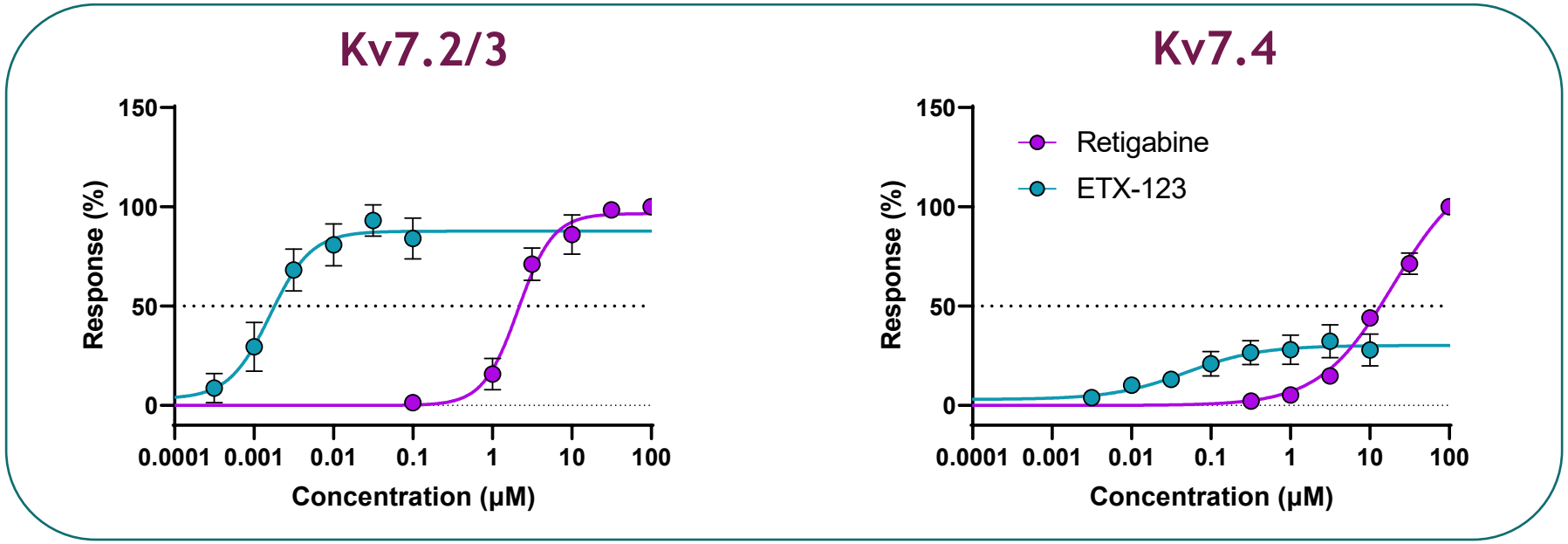
afterhyperpolarization

Discovery and optimization: leveraged existing target knowledge and deep ion channel expertise to identify novel class of Kv7 openers



ETX-123 selected as lead clinical candidate based on compelling potency, selectivity, and in vivo profile

Electrophysiology: ETX-123 demonstrates best-in-class Kv7.2/3 potency and selectivity

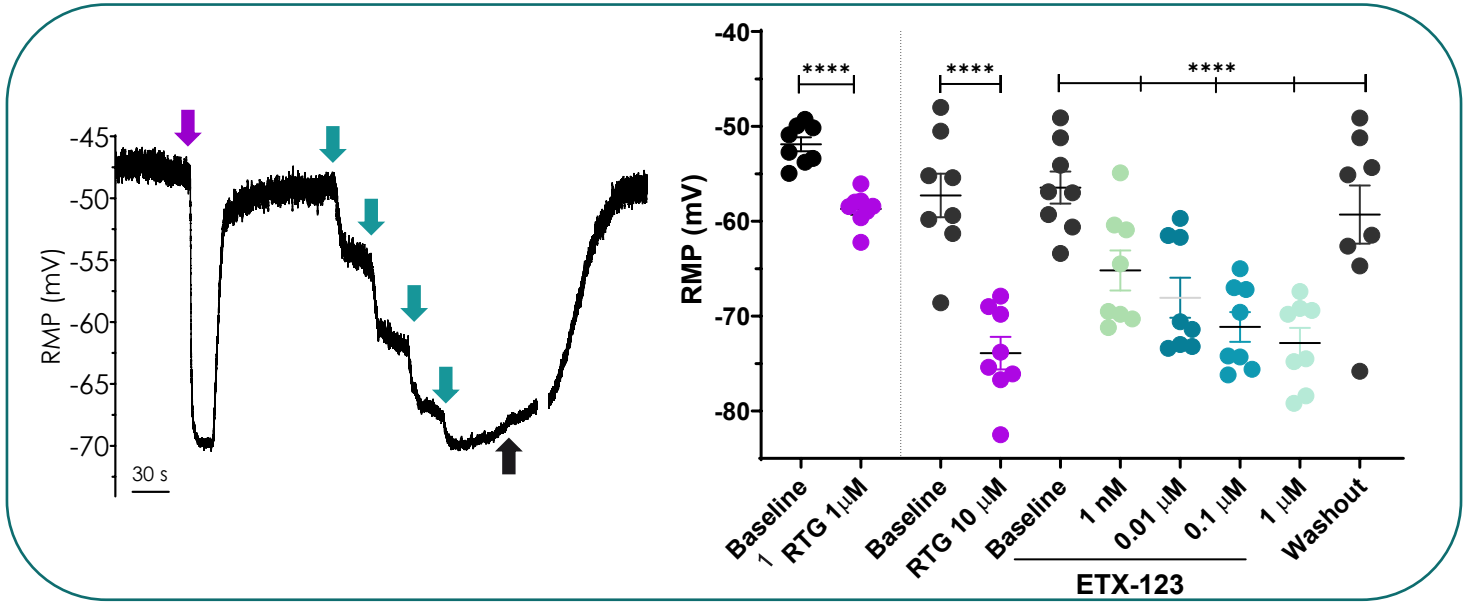


	ETX-123 (μM)	Retigabine (μM)
Kv7.2/3	0.0007-0.002	2
Kv7.4	>10	12-14
Kv7.3/5	0.02	4-7
Kv7.1	>30	>30*

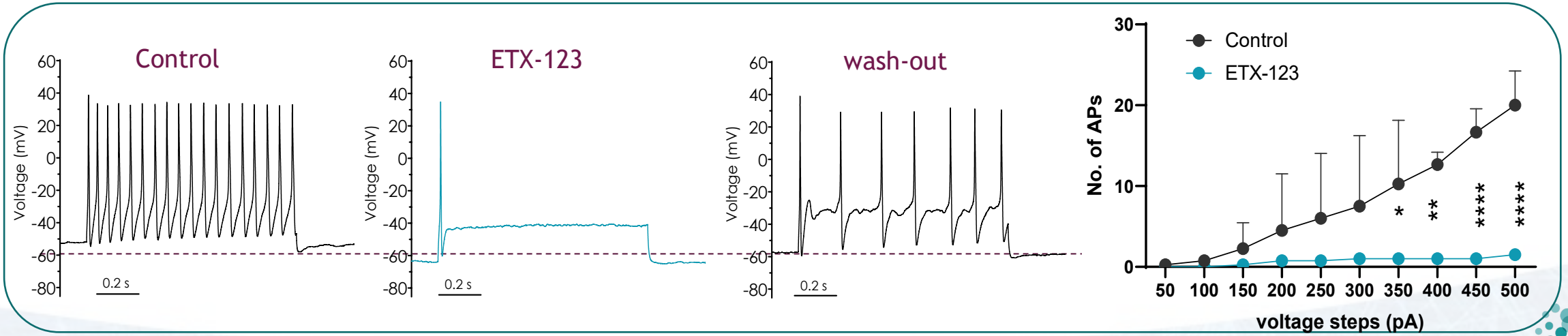
In vitro, ETX-123 is significantly more potent and selective than retigabine, and other published Kv7 openers

* Gunthorpe et al., 2012

Translational pharmacology: ETX-123 decreases rat DRGs excitability by hyperpolarization and significant inhibition of repeat firing of action potentials



[1] Free clinical anticonvulsant exposure



****p < 0.0001, **p < 0.01 and *p <0.05 - comparisons all groups vs. the control group

In vivo efficacy: ETX-123 showed dose-dependent anticonvulsant activity in the rat MES model, with encouraging separation vs doses showing CNS side effects in the rotarod model

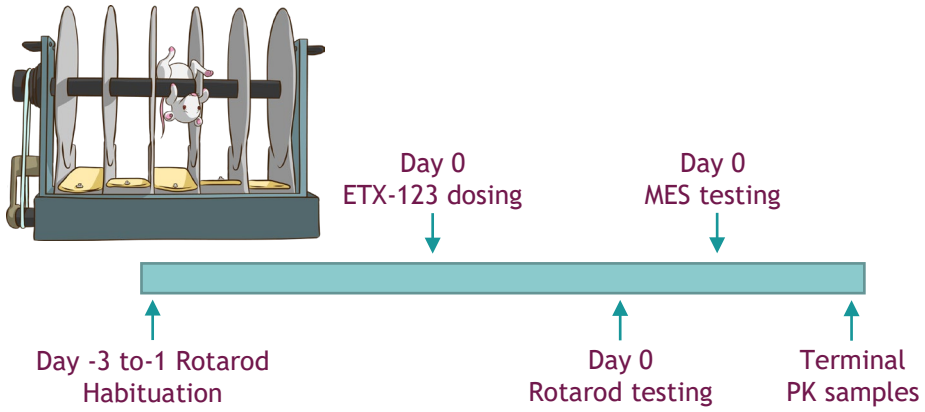
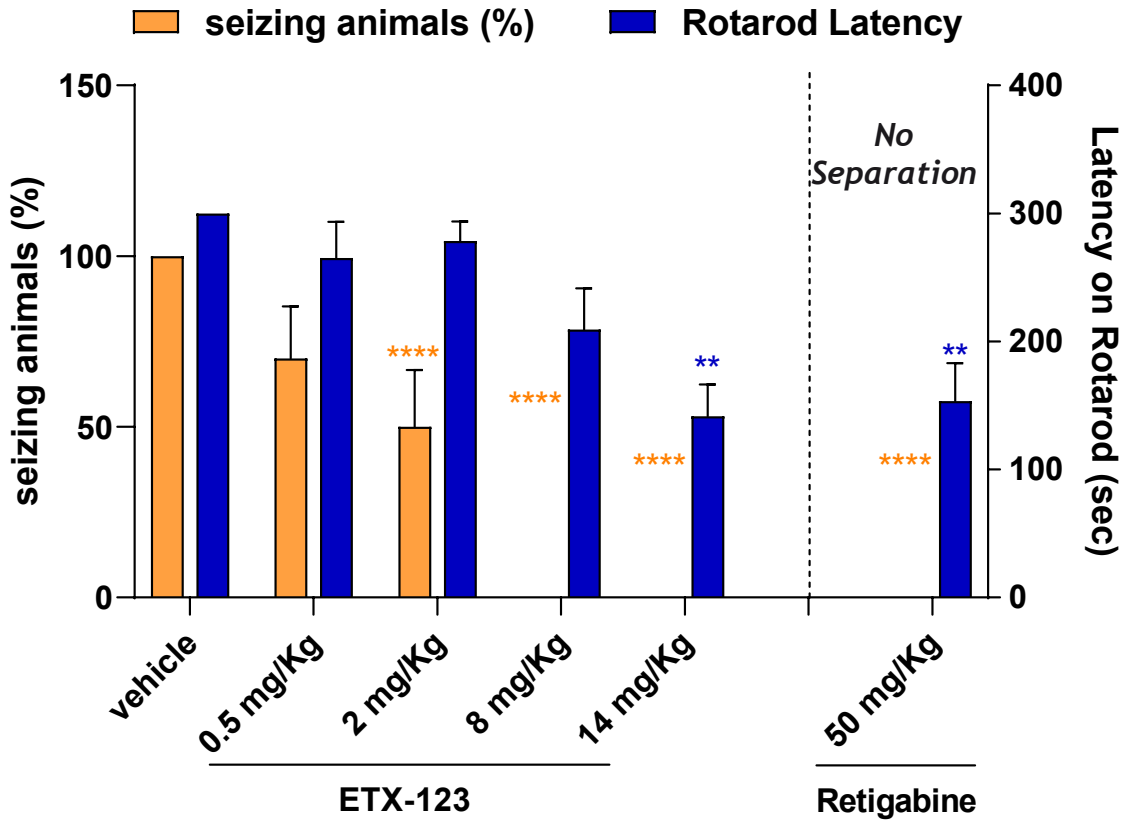


Image Source: https://conductscience.com/maze/maze-basics-rotarod-test-for-mice/

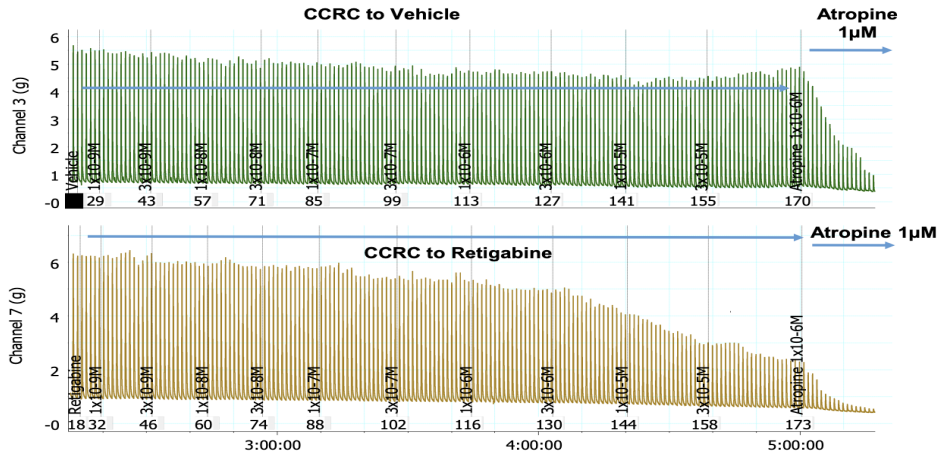


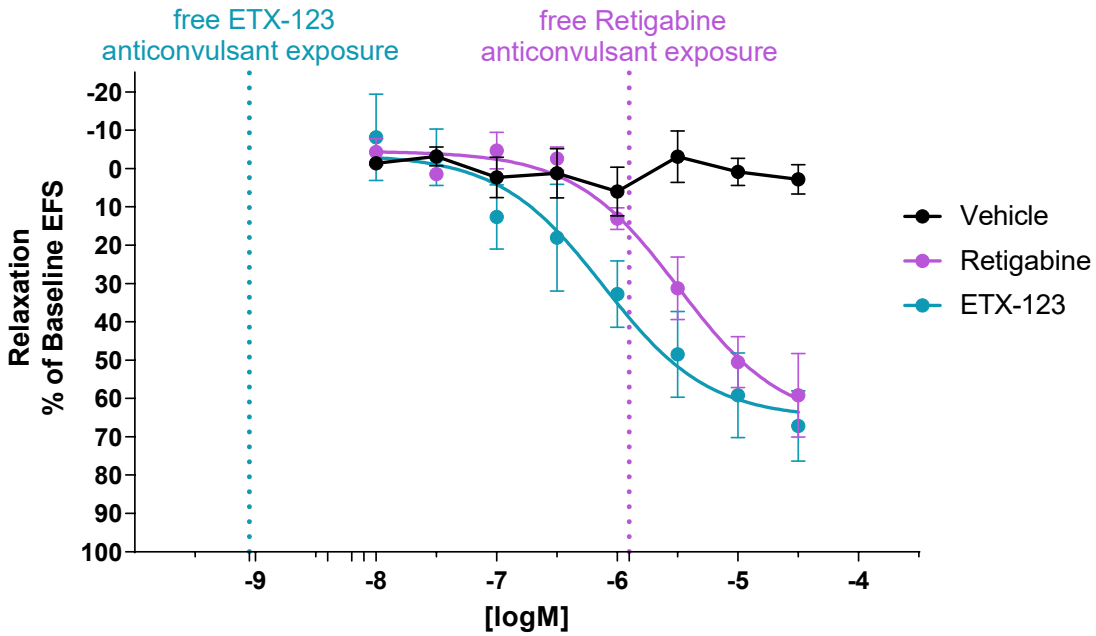
ETX-123 has demonstrated potent in vivo efficacy in a highly translatable model of epilepsy, along with a favorable tolerability profile

****p < 0.0001 and **p < 0.01 – comparisons all groups vs. respective vehicle for each variable

Human bladder contractility assay: Free anticonvulsant concentration of ETX-123 are >700-fold lower than concentration relaxing human bladder, vs only ~4-fold for retigabine

Contraction of human bladder strips evoked by electrical field stimulation (EFS) of endogenous nerves

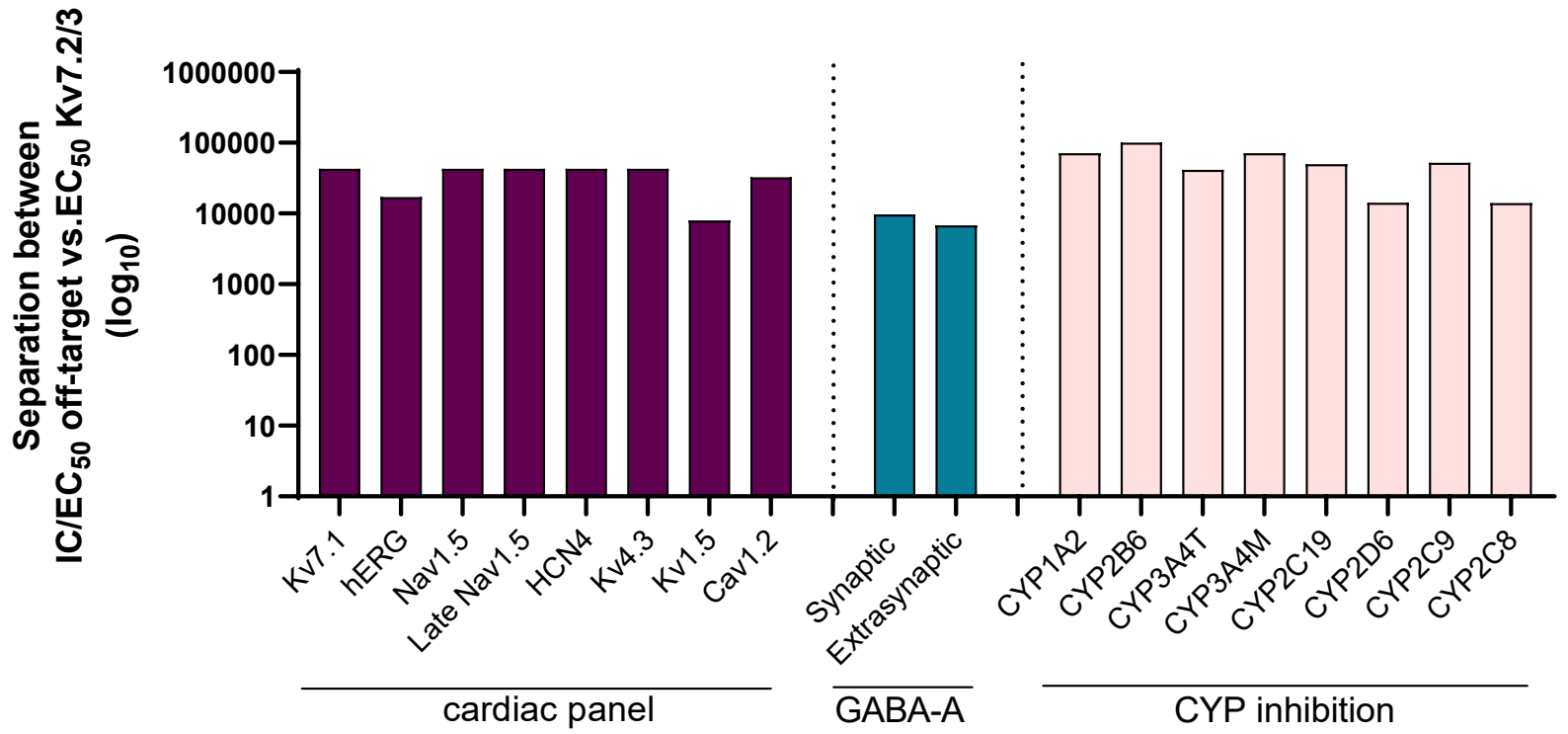




- Urinary retention adverse events, or related voiding dysfunctions were reported with retigabine/ezogabine in 2% of patients
- Activity at Kv7.4 in the bladder smooth muscle is a key factor

ETX-123 performance vs retigabine/ezogabine in human bladder translational assay is encouraging ahead of clinical studies

Broad Selectivity: multiple screens confirm no off-target activity



ETX-123 shows at least a >1000-fold separation vs. Kv7.2/3 EC_{50} in multiple screen, including a 48-Target Cerep screening panel

ETX-123 profile to date is significantly superior to retigabine

	ETX-123 (pre-formulation*)	Retigabine
In vitro profile		
Potency at Kv7.2/3	0.7- 2 nanoM	2-14 microM
Selectivity over Kv7.1		
Selectivity over Kv7.4	>14,000-fold selectivity	Poor selectivity
Metabolite profile	*In vitro*	Toxic azoquinones
In vivo profile		
Rat MES		
Separation in Rat MES vs rotarod		No separation
Chemistry		
Structural features	Novel scaffold, not disclosed	Substituted aniline
IP	COM IP Filed August 2022	n/a (off-market)

* ETX-123 data before formulation optimized to improve solubility and oral bioavailability

Progressing ETX-123 through IND-enabling activities in 2023, with Phase 1 anticipated to begin in 1H 2024

Key activities	Status
Novel “non-retigabine” chemotype (COM IP filed August 22)	✓
Potency and selectivity	✓
No off-target activity (GABA, hERG, CEREP receptor panel)	✓
No genotoxicity risk with Ames test	✓
Confirmation of therapeutic window in preclinical pharmacology and safety studies	Ongoing
Initiate Phase 1 in healthy subjects, including TMS *to confirm target engagement at target clinical dose*	1H 2024

Opportunity to pursue multiple neuronal excitability indications in Phase 2 and beyond

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