UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 5, 2022

ELIEM THERAPEUTICS, INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware	001-40708	83-2273741
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

23515 NE Novelty Hill Road, Suite B221#125 Redmond, WA	98053
(Address of Principal Executive Offices)	(Zip Code)

Registrant's Telephone Number, Including Area Code: (425) 276-2300

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	**ELYM**	**The Nasdaq Stock Market LLC (The Nasdaq Global Market)**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02. Results of Operations and Financial Condition.

On October 5, 2022, Eliem Therapeutics, Inc. (Eliem, or the Company) issued a press release providing program updates, announcing expected upcoming milestones and providing an update on the Company's unaudited cash, cash equivalents and marketable securities as of September 30, 2022. In such press release, the Company reported that its unaudited cash, cash equivalents and marketable securities were approximately $129.8 million as of September 20, 2022, which amount includes the receipt of $6.2 million in tax reimbursements in the third quarter of 2022. A copy of such press release is attached to this Current Report as Exhibit 99.1.

Item 7.01. Regulation FD Disclosure.

A copy of a slide presentation that Eliem will use at investor conferences and presentations is attached to this Current Report as Exhibit 99.2 and is incorporated herein solely for purposes of this Item 7.01 disclosure.

The information in Items 2.02 and 7.01 (including Exhibits 99.1 and 99.2) is being furnished, not filed, for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any filing under the Exchange Act or the Securities Act of 1933, as amended, whether filed before or after the date hereof and regardless of any general incorporation language in such filing.

Item 8.01. Other Events.

Program Updates and Anticipated Key Milestones

Eliem also provided the following program updates and announced expected upcoming milestones.

ETX-155 Program: ETX-155 is a novel $GABA_A$ receptor positive allosteric modulator ($GABA_A$ PAM) that is being developed for the treatment of major depressive disorder (MDD) and epilepsy. Following the observation of lower-than-expected drug exposure levels in the three subjects evaluated in a Phase 1b photosensitive epilepsy (PSE) trial, the Company initiated a Phase 1, single and repeat dose, clinical trial in healthy subjects to confirm the pharmacokinetic profile of ETX-155 in advance of a planned Phase 2a clinical trial in subjects with MDD. The drug exposure levels from the recently executed single dose part of the Phase 1 pharmacokinetic trial (N=42) were compared with the population pharmacokinetic model built with data from healthy subjects evaluated in the original, previously disclosed Phase 1 trials (N=70). Results demonstrated that at the 60-milligram dose, there was no meaningful difference between exposures obtained with different batches, and that the low exposures observed in the Phase 1b PSE trial are within the range of previously reported moderate variability. In addition, and upon extensive investigation, no irregularities or differences were observed with chemistry, manufacturing, and controls (CMC) associated with the drug product and the drug substance batches used in the PSE trial or with other newly produced drug substance and product.

Given the encouraging safety, tolerability, and pharmacokinetic profile of the 60-milligram dose in the prior two Phase 1 repeat dose trials and well-tolerated single dose data with a 75-milligram dose in the ongoing Phase 1 pharmacokinetic trial, the Company plans to evaluate a 75-milligram dose of ETX-155 in the repeat dose part of the ongoing Phase 1 pharmacokinetic trial in healthy subjects prior to making a decision on the dose for the planned Phase 2a MDD trial. Final results from the Phase 1 pharmacokinetic trial, including the repeat dose cohort, are expected in the fourth quarter of 2022. The Company currently anticipates initiating the Phase 2a MDD trial in the first quarter of 2023 using either the 60-milligram or 75-milligram dose of ETX-155, depending on the final exposure, safety and tolerability results from the ongoing Phase 1 pharmacokinetic trial. Assuming initiation in the first quarter of 2023, the topline data for the Phase 2a MDD trial would be expected in mid-2024.

The Company also has determined it will not reinitiate the PSE proof-of-concept trial but will continue to pursue development of ETX-155 in focal onset seizures (FOS), given existing clinical validation of the $GABA_A$ PAM mechanism in this indication.

Kv7.2/3 channel opener program: The Company's preclinical program targets the Kv7.2/3 potassium channel (Kv7), a target that has clinical validation in pain and epilepsy. The Company has filed foundational intellectual property claims on its novel Kv7 compounds. In addition, while pursuing further lead evaluation, the Company has initiated the scaling up of two pre-candidates to enable the initiation of IND-enabling safety studies, expected in the first quarter of 2023, with Phase 1 studies planned to initiate in the first half of 2024. The Company's novel Kv7 compounds have demonstrated high potency and differentiated selectivity in electrophysiology assays, and in vivo anticonvulsant activity in the maximal electroshock seizure (MES) rat model. Preclinical data on the Kv7 compounds are planned to be reported later in the fourth quarter of 2022.

Anxiolytic for generalized anxiety disorder (GAD): The Company has discontinued early preclinical development of a novel, non-sedating anxiolytic for the potential treatment of GAD because none of the compounds investigated achieved the required profile.

Forward-Looking Statements

Statements in this report that are not statements of historical fact are forward-looking statements, including, without limitation, statements relating to: the advancement of Eliem's pipeline; the continued development and clinical and therapeutic potential of ETX-155 and Eliem's Kv7.2/3 channel opener program; Eliem's plan to study a 75-milligram repeat dose in the ongoing Phase 1 pharmacokinetic trial of ETX-155 and expected timing for the availability of final results from that trial; Eliem's belief that it is positioned to commence the referenced phase 2a trial of MDD in the first quarter of 2023; Eliem's plans to continue to pursue development of ETX-155 in focal onset seizures; Eliem's planned activities and expectations for the Kv7.2/3 channel opener program, including the initiation of Phase 1 studies, and the timing thereof; Eliem's plans to report preclinical data on the Kv7 program later in the fourth quarter of 2022; and Eliem's commitment to developing therapies targeting neuronal excitability disorders. Words such as "advancing," "anticipates," "assuming," "believe," "compelling," "continue," "excited," "expected," "focus," "initiate," "on track," "plans," "positioned," "potential," "progress," "pursue," "will," "would," or other similar expressions, identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. The forward-looking statements in this press release are based upon Eliem's current plans, assumptions, beliefs, expectations, estimates and projections, and involve substantial risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in the forward-looking statements due to these risks and uncertainties as well as other factors, which include, without limitation: the clinical, therapeutic and commercial value of ETX-155 and the Kv7 program; risks related to the potential failure of ETX-155 or the Kv7 program to demonstrate safety and efficacy in clinical testing; Eliem's ability to initiate and conduct clinical trials and studies of ETX-155 or the Kv7 program sufficient to achieve a positive completion; the availability of data at the expected times; Eliem's ability to obtain and protect intellectual property rights, and operate without infringing on the intellectual property rights of others; the uncertain timing and level of expenses associated with Eliem's preclinical and clinical development activities; the sufficiency of Eliem's capital and other resources; risks and uncertainties related to regulatory application, review and approval processes and Eliem's compliance with applicable legal and regulatory requirements; market competition; changes in economic and business conditions; impacts on Eliem's business due to external events, including health pandemics or other contagious outbreaks, such as the current COVID-19 pandemic; and other factors discussed under the caption "Risk Factors" in Eliem's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2022. The forward-looking statements made in this report speak only as of the date of report. Eliem expressly disclaims any duty, obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in Eliem's expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press release of Eliem Therapeutics, Inc., dated October 5, 2022
99.2	Investor Presentation dated October 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Eliem Therapeutics, Inc.

Date: October 5, 2022

By: /s/ James B. Bucher

James B. Bucher
Executive Vice President and General Counsel

Exhibit 99.1

Eliem Therapeutics Provides Update on Pipeline Progress

Company is positioned to initiate Phase 2a trial in major depressive disorder (MDD) in the first quarter of 2023

ETX-155 demonstrating exposures in single dose 60-milligram cohorts of ongoing Phase 1 pharmacokinetic trial that are consistent with prior clinical trials

Progressing into IND-enabling studies for two Kv7 pre-candidates

SEATTLE and CAMBRIDGE, United Kingdom, Oct. 05, 2022 (GLOBE NEWSWIRE) — Eliem Therapeutics, Inc. (Nasdaq: ELYM), a clinical-stage biotechnology company focused on developing novel therapies for neuronal excitability disorders to address unmet needs in psychiatry, epilepsy, chronic pain, and other disorders of the peripheral and central nervous systems, today provided an update on its pipeline programs, including the announcement of interim results from its ongoing Phase 1 clinical trial of ETX-155.

"I am tremendously grateful for the extraordinary effort put forth by our team to bring the ETX-155 program back on track while taking the time to understand the pharmacokinetic profile in order to have the right exposure levels to progress to Phase 2a. Based on the compound's favorable safety, tolerability, pharmacokinetic profile, and preclinical efficacy to date, we believe we are now well positioned to evaluate the efficacy and safety of ETX-155 in patients with MDD, which represents an important milestone for Eliem," said Bob Azelby, chief executive officer of Eliem Therapeutics. "We are also very excited about advancing two pre-candidates from our Kv7 program into IND-enabling studies. Both ETX-155 and Kv7 represent compelling product opportunities with the potential to be clinically differentiated drugs within classes where there is strong precedent clinical validation in depression and epilepsy, respectively. We remain well capitalized to bring these programs through key clinical data catalysts."

ETX-155 program: ETX-155 is a novel $GABA_A$ receptor positive allosteric modulator ($GABA_A$ PAM) that is being developed for the treatment of major depressive disorder (MDD) and epilepsy. Following the observation of lower-than-expected drug exposure levels in the three subjects evaluated in a Phase 1b photosensitive epilepsy (PSE) trial, the Company initiated a Phase 1, single and repeat dose, clinical trial in healthy subjects to confirm the pharmacokinetic profile of ETX-155 in advance of a planned Phase 2a clinical trial in subjects with MDD. The drug exposure levels from the recently executed single dose part of the Phase 1 pharmacokinetic trial (N=42) were compared with the population pharmacokinetic model built with data from healthy subjects evaluated in the original, previously disclosed Phase 1 trials (N=70). Results demonstrated that at the 60-milligram dose, there was no meaningful difference between exposures obtained with different batches, and that the low exposures observed in the Phase 1b PSE trial are within the range of previously reported moderate variability. In addition, and upon extensive investigation, no irregularities or differences were observed with chemistry, manufacturing, and controls (CMC) associated with the drug product and the drug substance batches used in the PSE trial or with other newly produced drug substance and product.

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The Company also has determined it will not reinitiate the PSE proof-of-concept trial but will continue to pursue development of ETX-155 in focal onset seizures (FOS), given compelling existing clinical validation of the $GABA_A$ PAM mechanism in this indication.

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Anxiolytic for generalized anxiety disorder (GAD): The Company has discontinued early preclinical development of a novel, non-sedating anxiolytic for the potential treatment of GAD because none of the compounds investigated achieved the required profile.

Cash position: The Company's unaudited cash, cash equivalents, and investments as of September 30, 2022 were $129.8 million, including receipt of $6.2 million in tax reimbursements within the quarter, which is expected to fund operations into 2025.

About Eliem Therapeutics, Inc.

Eliem Therapeutics, Inc. is a clinical-stage biotechnology company focused on developing novel therapies for neuronal excitability disorders to address unmet needs in psychiatry, epilepsy, chronic pain, and other disorders of the peripheral and central nervous systems. These disorders often occur when neurons are overly excited or inhibited, leading to an imbalance, and our focus is on restoring homeostasis. We are developing a pipeline of clinically differentiated product candidates focused on validated mechanisms of action with broad therapeutic potential to deliver improved therapeutics for patients with these disorders. Eliem channels its experience, energy, and passion for improving patients' quality of life to fuel our efforts to develop life-changing novel therapies. At its core, the Eliem team is motivated by the promise of helping patients live happier, more fulfilling lives. https://eliemtx.com/

Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements relating to: the advancement of Eliem's pipeline; the continued development and clinical and therapeutic potential of ETX-155 and Eliem's Kv7.2/3 channel opener program; Eliem's plan to study a 75-milligram repeat dose in the ongoing Phase 1 pharmacokinetic trial of ETX-155 and expected timing for the availability of final results from that trial; Eliem's belief that it is positioned to commence the referenced Phase 2a trial of MDD in the first quarter of 2023; Eliem's plans to continue to pursue development of ETX-155 in focal onset seizures; Eliem's planned activities and expectations for the Kv7.2/3 channel opener program, including the initiation of Phase 1 studies, and the timing thereof; Eliem's plans to report preclinical data on the Kv7 program later in the fourth quarter of 2022; Eliem's belief that ETX-155 and Kv7 represent compelling product opportunities with the potential to be clinically differentiated drugs; Eliem's belief that it is well capitalized and that its current cash, cash equivalents and short- and long-term marketable securities will fund operations into 2025; and Eliem's commitment to developing therapies targeting neuronal excitability disorders. Words such as "advancing," "assuming," "believe," "compelling," "continue," "excited," "expected," "focus," "initiate," "on track," "plans," "positioned," "potential," "progress," "pursue," "will," "would," or other similar expressions, identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. The forward-looking statements in this press release are based upon Eliem's current plans, assumptions, beliefs, expectations, estimates and projections, and involve substantial risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in the forward-looking statements due to these risks and uncertainties as well as other factors, which include, without limitation: the clinical, therapeutic and commercial value of ETX-155 and the Kv7 program; risks related to the potential failure of ETX-155 or the Kv7 program to demonstrate safety and efficacy in clinical testing; Eliem's ability to initiate and conduct clinical trials and studies of ETX-155 or the Kv7 program sufficient to achieve a positive completion; the availability of data at the expected times; Eliem's ability to obtain and protect intellectual property rights, and operate without infringing on the intellectual property rights of others; the uncertain timing and level of expenses associated with Eliem's preclinical and clinical development activities; the sufficiency of Eliem's capital and other resources; risks and uncertainties related to regulatory application, review and approval processes and Eliem's compliance with applicable legal and regulatory requirements; market competition; changes in economic and business conditions; impacts on Eliem's business due to external events, including health pandemics or other contagious outbreaks, such as the current COVID-19 pandemic; and other factors discussed under the caption "Risk Factors" in Eliem's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2022. This filing is available on the SEC's website at www.sec.gov. Additional information will also be set forth in Eliem's other reports and filings it will make with the SEC from time to time. The forward-looking statements made in this press release speak only as of the date of this press release. Eliem expressly disclaims any duty, obligation or undertaking to release publicly any updates or revisions to any forward-looking

statements contained herein to reflect any change in Eliem's expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

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Exhibit 99.2

Clinical Stage Neurology Company Focused on Neuronal Excitability Disorders

Corporate Presentation | October 5, 2022

eliem Therapeutics

Forward-Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potentially," "predict," "should," "will" or the negative of these terms or other similar expressions. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things, risks related to: the success, cost and timing of our product development activities and clinical trials; our expectations about the timing of achieving regulatory approval and the cost of our development programs; our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates; the impact of the COVID-19 pandemic on our operations; the commercialization of our product candidates, if approved; our plans to research, develop and commercialize our product candidates; our plans to develop additional product candidates; our ability to obtain, maintain, expand, protect and enforce our intellectual property rights; our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights of third parties; our ability to attract collaborators with development, regulatory and commercialization expertise; future agreements with third parties in connection with the commercialization of our product candidates; the size and growth potential of the markets for our product candidates and our ability to serve those markets; the rate and degree of market acceptance of our product candidates; regulatory developments in the United States and foreign countries; regulatory application, review and approval processes and our compliance with applicable legal and regulatory requirements; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; the success of competing products that are or may become available; and our ability to attract and retain key scientific or management personnel. These risks are not exhaustive. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. More information about the risks and uncertainties faced by Eliem is contained under the caption "Risk Factors" set forth in Eliem's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2022, which is available on the SEC's website at www.sec.gov, and in other subsequent reports and filings Eliem will make with the SEC from time to time. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

Certain information contained in this presentation relates to, or is based on, studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

Rethinking treatment for nervous system disorders

- **Highly experienced** management team
- **Clinical and preclinical pipeline** based on clinically validated mechanisms of action
- **Two differentiated programs** in depression and epilepsy with expansion opportunities in chronic pain
- **~$130M* cash runway into 2025** allows for topline clinical data readouts and advancement of preclinical asset into clinic

* Unaudited cash, cash equivalents and investments as of September 30, 2022, including receipt of $6.2m in tax reimbursements within the quarter

Powered by successful and talented executives from pioneering organizations

General Management, Commercial & Corporate Development

Robert Azelby, MBA
Chief Executive Officer

Erin Lavelle
Chief Operating Officer & Chief Financial Officer

James Bucher, J.D.
EVP and General Counsel

Research & Development

Valerie Morisset, Ph.D.
EVP R&D and Chief Scientific Officer

Joanne Palmer, Ph.D.
Chief Development Officer

Mark Versavel, M.D., Ph.D.
Interim Chief Medical Officer

Deep expertise in neuroscience research, clinical development and commercialization

- Lyrica, Neurontin, Trobalt, Vyepti, Vixotrigine, Nimotop, Aptiom, Lunesta, Geodon

Leadership experience in both large pharma and small biotech

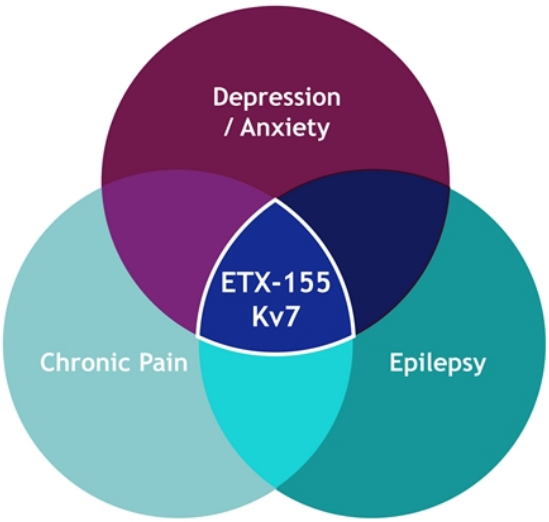
- Large: Amgen, GSK, Novartis, Biogen, Bayer, Pfizer
- Small: Alder, Juno, Convergence, Cavion, Exelixis

Highly skilled in public/private capital raising and corporate development with successful exits

- Exits: Alder, Convergence, Juno, Immunomedics, Cascadian, Cavion

eliem Therapeutics

Addressing multiple interrelated diseases with two distinct, clinically validated mechanisms of action



Approaching **interrelated disease states** with distinct MOAs ($GABA_A$ PAM and Kv7.2/3)

Innovating within **clinically validated** mechanisms of action

Multiple **"pipeline-in-a-product"** opportunities

Eliem Pipeline: Two programs with clinically validated MOAs intended to address large markets

Product Candidate (Mechanism)	Lead indications	Preclinical	Phase 1	Phase 2	Phase 3
ETX-155 ($GABA_A$ receptor PAM)	Major depressive disorder (MDD)			Positioned for Phase 2a initiation in Q1 2023	
	Epilepsy				
Kv7 Program (Kv7.2/3 channel opener)	Epilepsy Depression Pain		IND-enabling safety studies planned in Q1 2023		

$GABA_A$ PAM: $GABA_A$ receptor positive allosteric modulator

ETX-155

Proof of concept Phase 2a trial in Major Depressive Disorder (MDD) positioned for Q1 2023 initiation

ETX-155: A differentiated neuroactive steroid $GABA_A$ positive allosteric modulator

Clinical validation for MOA ($GABA_A$ PAM)

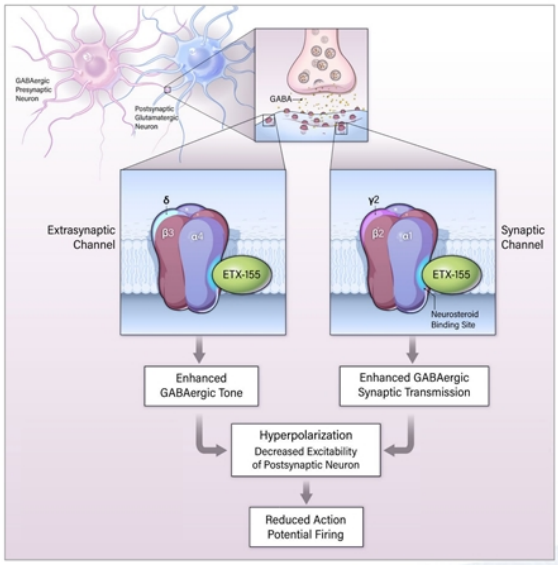
Dual potent activity at synaptic and extrasynaptic $GABA_A$ receptors, with high intrinsic efficacy

No clinically meaningful food effect

Convenient **once-daily dosing with ~40-hr half-life**

Well tolerated at exposure levels that have translated to clinical efficacy for other $GABA_A$ PAMs

Strong IP position with patent protection to 2039



Clinical development focused on MDD with opportunity to expand into other large markets with considerable unmet need

	Proof of concept planned	Potential future indication opportunities	
	 Major Depressive Disorder (MDD)	 Perimenopausal Depression (PMD)	 Epilepsy / Focal Onset Seizure (FOS)
MoA Rationale	• Reduced GABA levels → increased MDD severity[1] • Clinically validated (zuranolone)	• Reduced neurosteroid levels → PMD symptoms • Clinically validated in neurosteroid-driven PPD (zuranolone)	• GABAergic deficits → epileptic state • Clinically validated in orphan epilepsies (ganaxolone)
Unmet Needs	• Faster onset of action • Improved tolerability/efficacy • Novel MoAs	• Same as MDD • Novel MoAs directly addressing reduced neurosteroid levels	• Novel MoAs → better seizure control • Positive impact on mood as #1 comorbidity is depression[4]
Estimated annual prevalence (US+EU)	**~32m** (~9m failed ≥1 prior therapy)[2]	**~8m** (~2m with no history of MDD)[3]	**~2m** (~0.8m with uncontrolled seizures)[5]

1. Luscher et al, *Mol Psychiatry*, 2011;16(4):383-406
2. Decision Resources Group (DRG)- *Unipolar Depression Disease Landscape and Forecast*
3. Freeman et al, *JAMA Psychiatry*, 2014;72(1):36-43
4. Kanner AM, *Biol Psychiatry*, 2003;54(3):388-98
5. DRG - *Epilepsy Disease Landscape and Forecast*, May 2021

ETX-155 Differentiation: Similar dual $GABA_AR$ potency to clinically validated $GABA_A$ PAMs, with differentiated pharmacokinetics

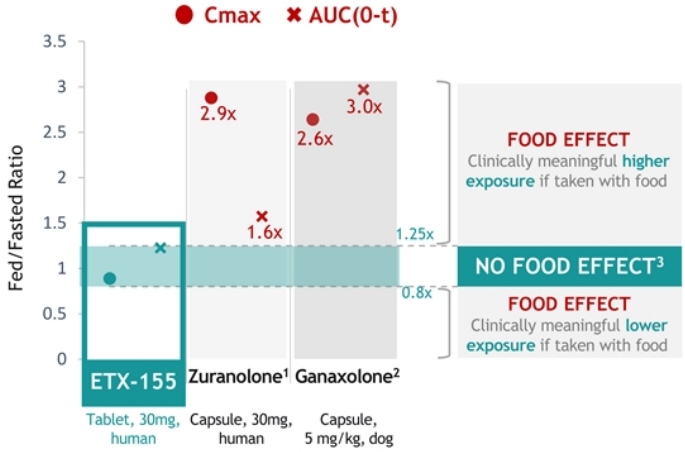
Company	Molecule	$GABA_AR$ Potency		Pharmacokinetics		Clinical Validation (positive RCT)		
		Synaptic	Extra-synaptic	Food effect	Half-life	MDD	PPD	Epilepsy
eliem Therapeutics	ETX-155	✓	✓	No	~40 hrs	-	-	-
Sage Therapeutics™	zuranolone (SAGE-217)	✓	✓	Yes	14-18 hrs	✓	✓	-
MARINUS PHARMACEUTICALS	ZTALMY® (ganaxolone)	✓	✓	Yes	2-3 hrs	-	-	✓

Sources:
Zuranolone: Hoffmann et al, *Clin Pharmacokinet*, 2020;59(1):111-120; Hoffmann et al, ASCP 2018, poster #782; Botella et al, *J Med Chem*, 2017;60(18)7810-7819; Phase 3 WATERFALL topline data press release
Ganaxolone: ZTALMY Prescribing Information; Hulihan et al., American Epilepsy Society Annual Meeting 2020, poster

* Evening QD dosing for ETX-155, zuranolone; TID dosing for ganaxolone

ETX-155 does not have a clinically meaningful food effect: potential to impact efficacy, safety, and compliance

Reported Fed/Fasted Ratios for $GABA_A$ PAM class



Presence of a food effect may impact:

Efficacy
Exposure reduced or increased if medication not taken with food

Safety and Tolerability
Timing/severity of AEs associated with Cmax

Compliance
More strict daily routine required to maintain drug levels within the required range for efficacy and safety

1. Hoffmann et al, Clin Pharmacokinet, 2020;59(1):111-120; Hoffmann et al, ASCP 2018, poster #782
2. U.S. Patent No. 9,029,355
3. Range of fed/fasted ratios for AUC and Cmax required to claim absence of food effect on bioavailability, per FDA Guidance For Industry, Food-Effect Bioavailability and Fed Bioequivalence Studies, December 2002

ETX-155 has not been assessed in a head-to-head study against zuranolone or ganaxolone, and the study designs and analytical methods for all product candidates may be different. As a result, such data may not be directly comparable.

Phase 1 Study in Healthy Subjects: Encouraging safety & tolerability profile observed with no severe or serious adverse events

Most common treatment-emergent AEs

(In ≥10% of ETX-155 treated subjects across repeat dose studies)

	7-day Repeat Dose		14-day Repeat Dose		Combined	
	ETX-155 60 mg (n=9)	Placebo (n=6)	ETX-155 60 mg (n=15)	Placebo (n=5)	ETX-155 60 mg (n=24)	Placebo (n=11)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
≥1 TEAE	**5 (56)**	3 (50)	**9 (60)**	4 (80)	**14 (58)**	7 (64)
Somnolence	**1 (11)**	2 (33)	**6 (40)**	2 (40)	**7 (29)**	4 (36)
Fatigue	**0**	0	**4 (27)**	1 (20)	**4 (17)**	1 (9)
Headache	**2 (22)**	2 (33)	**1 (7)**	0	**3 (13)**	2 (18)
Dizziness	**1 (11)**	0	**2 (13)**	0	**3 (13)**	0

ETX-155 Phase 1 Repeat-Dose Results

- **Favorable pharmacokinetics**
  - Steady state reached at day 8
  - ~40-hour half-life at steady state
- **60 mg evening dosing was well tolerated**
  - **No SAEs or discontinuations**
  - **All AEs were mild/moderate** and transient
- **CNS AE details**
  - **The rate of CNS AEs were comparable in ETX-155 and placebo groups**
  - Most CNS AEs occurred at Tmax (3-4 hrs post-dose)
  - **7 reports of somnolence** out of 24 ETX-155-treated patients (**no subject reported somnolence more than once** during dosing period)
  - Leeds Sleep Evaluation Questionnaire indicates **no difference in next-morning alertness or disruption in sleep quality** compared to placebo

Analysis of ETX-155 pharmacokinetic profile confirmed comparable 60mg exposures obtained with different batches, enabling path forward in Phase 2a MDD trial

Original Phase 1 studies

- **SAD** (5-200mg, n=6 active/cohort)
- **MAD 7-day** (60mg AM and PM, n=9 active/cohort)
- **MAD 14-day** (60mg PM, n=15 active/cohort)
- **Well tolerated**, especially with PM dosing
- **Encouraging PK profile**
  - Moderate CV% of ~30%
  - Half-life of ~40 hrs
  - Steady state at day 8
  - Moderate acc. ratio of ~2
  - No food effect
  - Exposures within preclinical efficacy range
- **Enabled selection of a Phase 2 clinical dose of 60mg**

PSE study findings (April '22)

- Proof-of-concept model in patients with photosensitive epilepsy (PSE)
- Single-dose of 135 mg ETX-155
- N=3 patients; evaluation of activity in this model was inconclusive due to ~50% lower-than-expected exposures
- Achievement of predicted therapeutic exposure levels is critical for success of planned Phase 2a MDD trial
- Prompted investigation to understand potential root causes prior to progressing to MDD trial

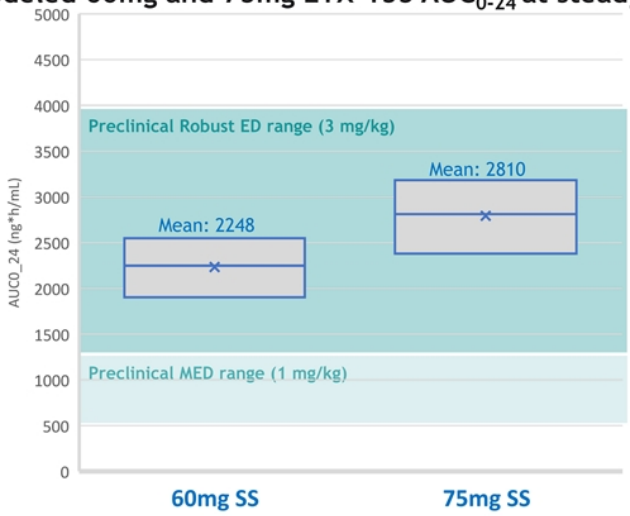
Extensive Investigation

1) CMC investigations on all batches of API and DP
   → No findings
2) Dog PK to compare preclinical exposure across all batches
   → Comparable across batches
3) 5 single dose cohorts of healthy subjects to confirm PK profile
   → Comparable exposure across batches
4) Comparison of exposures from all batches with population PK model based on original Phase 1 data
   → Exposures at 60mg fit the model
5) Confirmed 75mg well tolerated as a single-dose
   → Plan to evaluate 75mg in repeat-dose

Investigation concluded there was no meaningful difference between 60mg exposures obtained with different batches

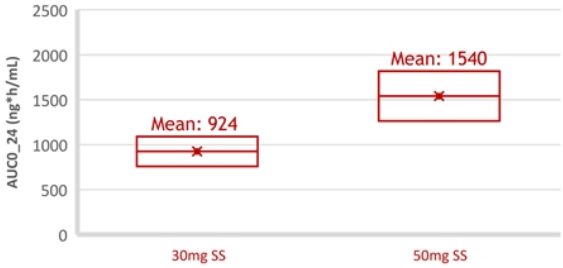
At steady-state, modeled exposures of ETX-155 60mg and 75mg doses are well within the therapeutic range

Modeled 60mg and 75mg ETX-155 AUC_{0-24} at steady state



Center lines represent the median, the top and bottom of the boxes represent the 25th and 75th percentiles (i.e. interquartile range)

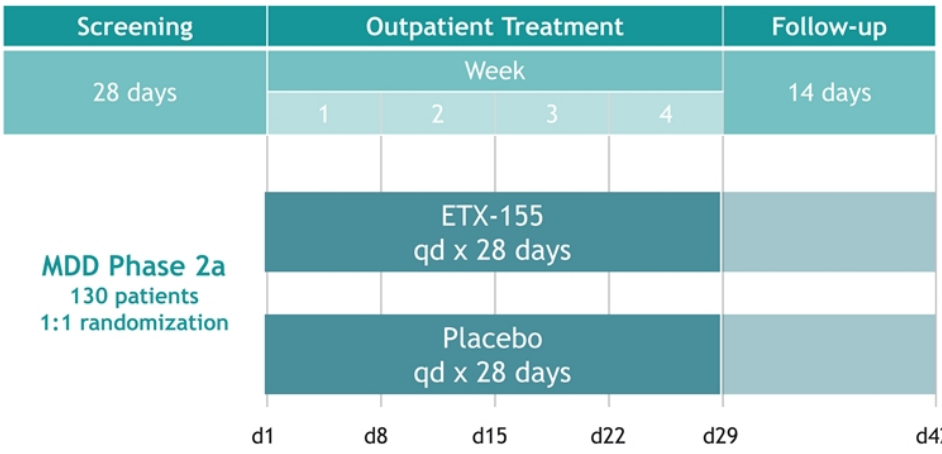
Benchmark zuranolone modeled AUC_{0-24} for 30mg and 50mg capsules at steady state*



* Derived from 30mg pharmacokinetic data in Bullock et al, Marcé of North America Congress, Oct 21-24, 2021, extrapolated to 50 mg based on dose linearity; modeled CV% derived from Hoffmann et al, 2018 Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, March 21-24, 2018

The two graphs are not generated from head-to-head trials and therefore are not direct comparisons. ETX-155 preclinical AUC ranges are derived from rat PK study for 1 mg/kg and 3 mg/kg groups, which were efficacious dose levels in depression, anxiety, seizure, and EEG preclinical models; ED: Efficacious Dose; MED: Minimal Efficacious Dose

Positioned to progress ETX-155 into Phase 2a RCT in MDD in Q1 2023 with topline data expected in mid-2024



Primary Endpoint

Change from baseline in HAMD17 over days 4, 8, 15, 22, and 29

Secondary Endpoints

Change from baseline in HAMD17 at days 4, 8, 15, 22, 29 and 42*

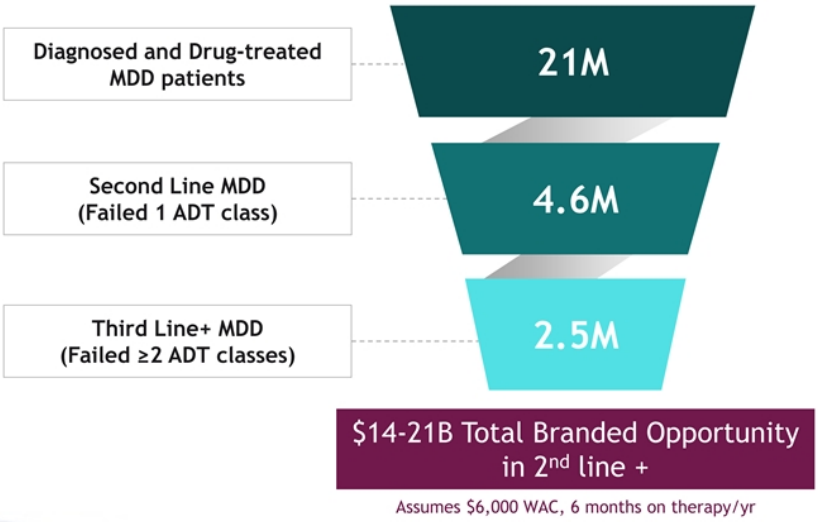
50% response rate in HAMD17 at days 4, 8, 15, 22, 29 and 42*

* Day 42 assessments are exploratory
HAMD17: Hamilton Depression Rating Scale

ETX-155 Market Opportunity

One-third (7M) of the US MDD treated patient opportunity is in 2nd line and beyond

US Epidemiology, 2030 estimates



$14-21B Total Branded Opportunity in 2nd line +

Assumes $6,000 WAC, 6 months on therapy/yr

Reference branded MDD drug peak sales

Drug	Class	Peak Sales	Peak Year
Lexapro	SSRI	$3.0B	2011
Effexor	SNRI	$2.7B	2008
Zoloft	SSRI	$2.6B	2005
Cymbalta	SNRI	$2.6B	2013
Prozac	SSRI	$2.4B	2001

Source: DRG Unipolar Depression Disease Landscape and Forecast, 2021

Zuranolone precedent $GABA_A$ PAM efficacy in line with approved MDD drugs, achieving statistical significance and ~50% reduction in HAMD17 despite smaller delta to placebo

Drug: Study*	Reference	Year of Study	Baseline HAMD17	Duration of Treatment	Mean HAMD17 change from Baseline			Estimated Mean HAMD17 at end of treatment	
					Active (top dose, if >1 arm)	Placebo	Delta to placebo	Active	Placebo
38 studies of SSRIs/SNRIs	Kirsch 2002	1980s-1990s	21.0 - 29.7	4-8 weeks	-10.4 (range: -5.9 to -14.2)	-7.6 (range: -3.0 to -10.5)	-2.8	~14	~17
Cymbalta: Study 1	Cymbalta label	2001	21	9 weeks	-10.9	-6.1	-4.9	10.1	14.9
Cymbalta: Study 2	Cymbalta label	2001	20	9 weeks	-10.5	-8.3	-2.2	9.5	11.7
Cymbalta: Study 3	Cymbalta label	2001	18	8 weeks	-8.6	-5.0	-3.6	9.4	13
Cymbalta: Study 4	Cymbalta label	2001	20	8 weeks	-12.1	-8.8	-3.3	7.9	11.2
Pristiq: Study 332	Liebowitz et al	2008	23	8 weeks	-11.5	-9.5	-2.0	11.5	13.5
Pristiq: Study 333	Boyer et al	2008	24	8 weeks	-13.7	-10.7	-3.0	10.3	13.3
Rexulti: Pyxis Study	Thase et al (a)	2013	21	6 weeks	-5.89	-3.59	-2.29	15.1	17.4
Rexulti: Polaris Study	Thase et al (b)	2013	21	6 weeks	-6.26	-4.57	-1.69	14.7	16.4
Rexulti: Sirius Study	Hobart et al	2016	21	6 weeks	-7.1	-5.9	-1.16	13.9	15.1
		Average of all drugs (range)		6-8 wks	-9.7 (-5.9 to -13.7)	-7.0 (-3.6 to -10.7)	-2.7 (-1.16 to -4.9)	11.6 (7.9 to 15.1)	14.4 (11.7 to 17.4)
Sage zuranolone data	Waterfall	2020-21	26.8	2 weeks	-14.1	-12.3	-1.7	12.7	14.6
	Coral	2021	26.8	2 weeks	-13.7	-12.9	-0.8	13.1	13.7

~50% reduction in mean HAMD17 from severe depression (>24) to mild depression (8-16)

* Studies reporting HAMD as primary endpoint shown here; recent MDD registrational trials for Trintellix, Spravato, and Axsome used MADRS as endpoint, rather than HAMD17, so are not included

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Zuranolone precedent suggests potential $GABA_A$ PAM advantages relative to existing ADTs: would be attractive in a "direct to patient" commercial marketplace

Background

- SSRI's treatment duration undefined – many patients on SSRIs for multiple years/life
- SSRI's can take 6 to 8 weeks to work, if they work; not accounting for titration period
- Side effects including weight gain, sexual dysfunction, withdrawal symptoms
- Unsatisfied market with new MDD patient on therapy for ~ 5.5 months, adherence rates of 51% at week 16, 21% at week 33[1]

Potential Differentiation Points

- **"Treat depressive episode":** zuranolone uses a two-week regimen, 80% of patients needed only 4 weeks of therapy in a year
- **Rapid onset:** zuranolone achieved activity by day 3, with no titration, which should enable patient to know within two weeks if product is working
- **Transient side effects:** somnolence/fatigue but no weight gain, sexual dysfunction, or withdrawal observed in zuranolone trials
- **Enhanced adherence:** two-week course of therapy should dramatically improve adherence

Short treatment duration combined with rapid effect enables dosing aligned with the depressive episode

1. Sawada et al, BMC Psychiatry, 2009;9(38).

ETX-155: Being Developed as a Potentially Clinically Differentiated Oral Neuroactive Steroid

ETX-155 Opportunities

Improve Efficacy: Increasing AUC
- Absence of clinically meaningful food effect
- Significantly longer half-life
- Higher exposures observed at well tolerated doses

Improve Tolerability
- CNS AE rates similar to placebo in healthy subjects
- No difference from placebo in sleep quality and next day alertness
- No reports of somnolence on more than one day in repeat dosing studies

Improve Durability
- Evaluate longer dosing regimens (i.e., 28 days)

Statements are not based on data resulting from head-to-head trials and are not direct comparisons of safety or efficacy

Kv7 Opener

Pre-candidates identified
IND-enabling safety studies planned for Q1 2023

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

Kv7 Opportunity

Human genetic validation

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

Metabolic/safety liabilities with existing molecules

Clear translational path to clinical efficacy

Eliem Kv7 Program Goal

Maintain efficacy with improved tolerability and safety

Program Status

- Foundational IP filed
- Multiple lead and backup candidates in novel chemical space
- Improved metabolic stability
- Potent at Kv7.2/3, selective vs Kv7.1/4, and active in MES rat model

Two pre-candidates being scaled up for IND-enabling safety studies anticipated to initiate in Q1 2023

MES: maximal electroshock seizure

Rethinking treatment for nervous system disorders

- **Highly experienced** management team
- **Clinical and preclinical pipeline** based on clinically validated mechanisms of action
- **Two differentiated programs** in depression and epilepsy with expansion opportunities in chronic pain
- **~$130M* cash runway into 2025** allows for topline clinical data readouts and advancement of preclinical asset into clinic

* Unaudited cash, cash equivalents and investments as of September 30, 2022, including receipt of $6.2m in tax reimbursements within the quarter

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