Topline Data from Phase 2 IRIS Trial Evaluating ML-004 in Autism Spectrum Disorder

June 22, 2026

Safe Harbor and Forward-Looking Statements

This presentation and any accompanying oral commentary have been prepared by MapLight Therapeutics, Inc. ("MapLight", "we," "us," "our," the "Company", or similar terms) for informational purposes only and not for any other purpose.

This presentation contains trademarks, service marks, trade names and copyrights of MapLight and other companies which are the property of their respective owners. This presentation discusses product candidates that are under pre-clinical and clinical study, and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or efficacy of these product candidates for the uses for which they are being studied.

Statements contained in this presentation and the accompanying oral commentary, other than statements of historical facts, may be forward-looking statements, including, but not limited to statements about the clinical development and potential benefits of ML-004 and the potential patient population for ML-004. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expects," "plans," "anticipates," "could," "intends," "targets," "projects," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. These statements involve substantial known and unknown risks, uncertainties and other factors that may cause our actual results, timing of results, levels of activity, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements. Risks and uncertainties that may cause actual results to differ materially include risks and uncertainties that are described in the "Risk Factors" section of our Quarterly Report on Form 10-Q with the U.S. Securities and Exchange Commission ("SEC") on May 14, 2026 and other filings we make with the SEC from time to time. These documents are available under the "SEC Filings" page of the "Investors" section of our website at www.maplightrx.com.

New risks emerge from time to time. It is not possible for our management to predict all risks, 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 and adversely from those anticipated or implied in the forward-looking statements. We may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. Except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements in this presentation and the accompanying oral commentary. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Agenda

Executive Summary and Key Takeaways for ML-004	Chris Kroeger, M.D.	Co-Founder and Chief Executive Officer
Phase 2 IRIS Study Results	Erin Foff, M.D., Ph.D.	Chief Medical Officer
Unmet Medical Need in ASD Irritability	Chris Kroeger, M.D.	Co-Founder and Chief Executive Officer
Closing Remarks	Chris Kroeger, M.D.	Co-Founder and Chief Executive Officer
Q&A Session	All	

Summary of IRIS Phase 2 Topline Results

Program Rationale

- **ML-004 is an IR/ER reformulation of the 5-$HT_1B/_1D$ agonist zolmitriptan**
  - Zolmitriptan demonstrates activity in both sociability and irritability/aggression animal models
    - Activation of 5-HT_1B receptors in the nucleus accumbens recapitulates the prosocial effects of MDMA
    - Aggression mechanism involves suppression of a subset of striatal D1-MSNs
- Based on preclinical findings, IRIS was designed as an exploratory study to evaluate multiple clinical endpoints in ASD

Efficacy Observations

- **IRIS (1) did not meet its primary endpoint in social communication deficits associated with ASD**
- **Clinically meaningful improvement observed in adolescents with moderate-to-severe baseline irritability (ABC-I ≥ 16) across both caregiver- and clinician-rated scales, despite small sample sizes**
  - A prespecified analysis in adolescents with baseline ABC-I ≥ 16 demonstrated meaningful improvement on the care partner-reported ABC-I vs. placebo at EOMD (ES of 1.33; nominal p=0.013)
  - Consistent with this finding, an analysis of the clinician-rated CGI-I Irritability in the same subpopulation demonstrated clinically meaningful improvement vs. placebo (ES of 1.08; nominal p=0.036)
  - Treatment effects were greater among adolescents with greater levels of baseline irritability

Safety and Tolerability

- **ML-004 was generally well-tolerated, with no severe or serious adverse events in the active treatment arm and potentially meaningful differentiation from standard of care atypical antipsychotics**
  - No extrapyramidal events were observed, and rates of sedation/somnolence were low
  - Mean weight gain was lower with ML-004 than with placebo

IR/ER = immediate release / extended release; MDMA = 3,4-methylenedioxymethamphetamine; ASD = autism spectrum disorder; ABC-I = Aberrant Behavior Checklist-Irritability; EOMD = end of maintenance dosing; ES = effect size; CGI-I = Clinical Global Impression-Improvement; 5-HT = 5-hydroxytryptamine (serotonin).

(1) Also known as ML-004-002 / NCT05081245.

Potential Future Development Considerations

Differentiation Opportunity	• Effect sizes observed in adolescents with moderate irritability are at/above those observed in clinical trials with antipsychotics currently approved for the treatment of irritability in ASD • Tolerability findings suggest potential differentiation from D_2-based atypical antipsychotics
Development Pathway	• FDA approval precedents support use of the ABC-I scale in this setting (1) • Following a full review of the data, the Company expects to engage with the FDA in an EOP2 meeting to determine the future development path
Meaningful Unmet Need	• The total addressable market for irritability in autism is large, and the unmet medical need remains high due to the limitations of existing therapies

Data support potential development of ML-004 for irritability associated with ASD, an indication with high unmet need and an established regulatory path; next steps will be guided by upcoming regulatory interactions

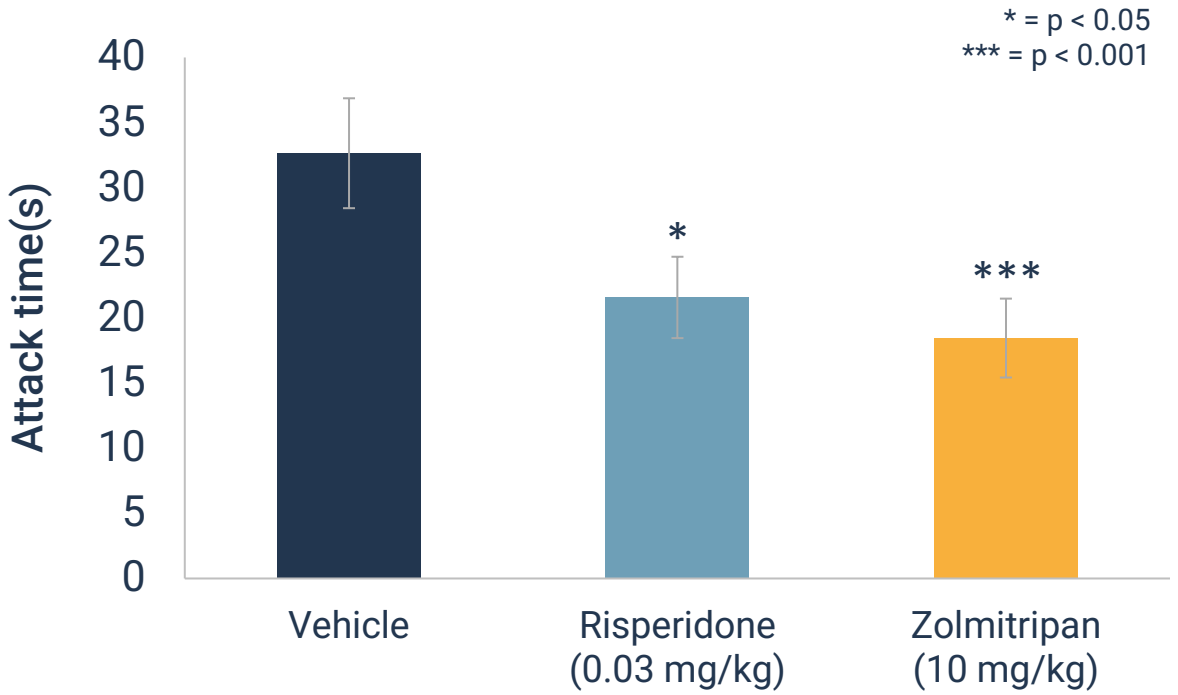
EOP2 = End-of-Phase 2; FDA = U.S. Food and Drug Administration.
(1) Approval precedents include risperidone, approved in 2006, and aripiprazole, approved in 2009, for irritability associated with ASD.

ML-004 Preclinical Findings in Aggression

Translational Rationale

- Decreased serotonin or loss of 5-HT_1B receptor function is linked to aggression in mice and humans (1)(2)(3)(4)
- Increased serotonin or activation of 5-HT_1B receptors inhibits brain circuits associated with aggression (2)
- At clinically-relevant exposures, zolmitriptan, the API of ML-004, reduces aggression in mice to a similar degree as risperidone, an approved treatment for irritability associated with ASD
- **These findings established the rationale for evaluating irritability-related behaviors in the Phase 2 IRIS study**

Resident Intruder Aggression Assay



ML-004 API

API = active pharmaceutical ingredient.

(1) Saudou et al, 1994
(2) Zhang et al, 2026
(3) Conner et al, 2010; Hakulinen et al, 2013
(4) da Cunha-Bang et al, 2017

Phase 2 Results

Erin Foff, M.D. | Chief Medical Officer

Phase 2 Study Background and Design

Background and Key Objectives

- IRIS was designed as an exploratory signal-finding study evaluating ML-004 in adolescents and adults with ASD
- Primary objective was to evaluate ML-004 vs. placebo for social communication deficits, a new indication for which there are no approved therapies
- Potential impact on irritability was a key secondary outcome measure due to strong preclinical findings
- **Study included several signal-finding considerations:**
  - Primary outcome measure without demonstrated treatment response: ABI-SC Domain Score
  - Flexible dosing allowing for exposure response analyses
  - Definition of positive efficacy signal: consistent, biologically plausible, and clinically coherent patterns across endpoints, not statistical significance alone

IRIS Study Design

- Multi-center, randomized, double-blind, placebo-controlled trial evaluating the efficacy, safety, and tolerability of ML-004
- **161 participants randomized 1:1 to ML-004 or placebo**
  - 102 adolescents ages 12-17; 59 adults ages 18-45
- **Once-daily oral bilayer IR/ER tablet formulation with flexible dosing paradigm**
  - Target maintenance dose of 48 mg or 72 mg, based on weight/contraceptive use (24 mg allowed based on tolerability)
- **Primary endpoint**: Change in ABI-SC Domain Score from baseline to end of maintenance dosing (EOMD) (1)
- **Key Secondary endpoints**:
  - CGI-I (global) and CFB to week 12 in the ABI-C
  - Change in ABC-I score from baseline to EOMD[1] for patients with ≥ moderate irritability at baseline

ABI-SC = Autism Behavioral Inventory-Social Communication; ABI-C = Autism Behavioral Inventory-Clinician Score; CFB = Change from Baseline; CGI-I = Clinician Global Impression-Improvement.
(1) Double-blind baseline to start of maintenance dosing was ~9-12 days; maintenance dose period was 12 weeks.

Efficacy Observations Across Endpoints

	Primary Endpoint	Key Secondary Endpoints			Other (1)
Scale	**ABI-SC**	**CGI-I**	**ABI-C**	**ABC-I**	**CGI-I Irritability**
Rater	Care-partner reported	Clinician-rated	Clinician-rated	Care-partner reported	Clinician-rated
Domain Assessed	Social Communication	Global Autism	Global Autism	Irritability (with baseline ABC-I≥16)	Irritability (with baseline ABC-I≥16)
Result	No statistical separation	No statistical separation	No statistical separation	**Overall:** Large ES of 0.64, not nominally statistically significant **Adolescents (Prespecified):** Clinically meaningful improvement vs. PBO → ES of 1.33, nominal p=0.013	**Overall:** Large ES of 0.61, not nominally statistically significant **Adolescents:** Clinically meaningful improvement vs. PBO → ES of 1.09, nominal p=0.036

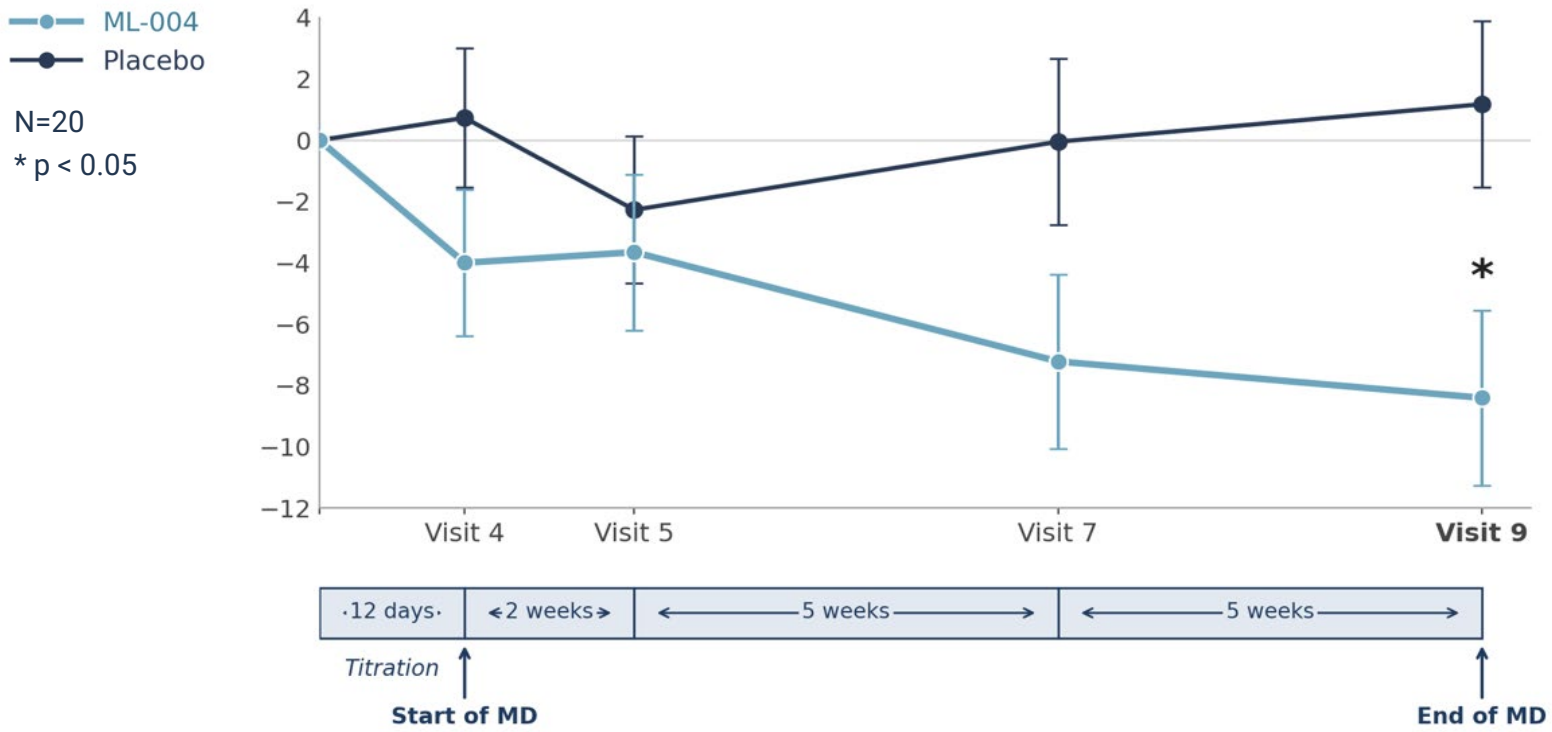
Greater treatment effect in adolescent participants with higher baseline severity

PBO = placebo.
(1) There were numerous protocol-defined secondary and exploratory endpoints.

ABC-I: Prespecified Adolescent Subgroup

Includes Subjects with ABC-I ≥16 at Baseline

Change From Baseline in ABC-I (LS Mean Difference)



	Visit 7	Visit 9
LS Mean Difference vs. PBO	-7.2	-9.6
P-value	0.052	0.013 *
Effect Size	1.00	1.33

- Numerical separation from PBO emerged early and increased through the end of maintenance dosing
- Large treatment effect at EOMD with a 9.6-point PBO-adjusted improvement

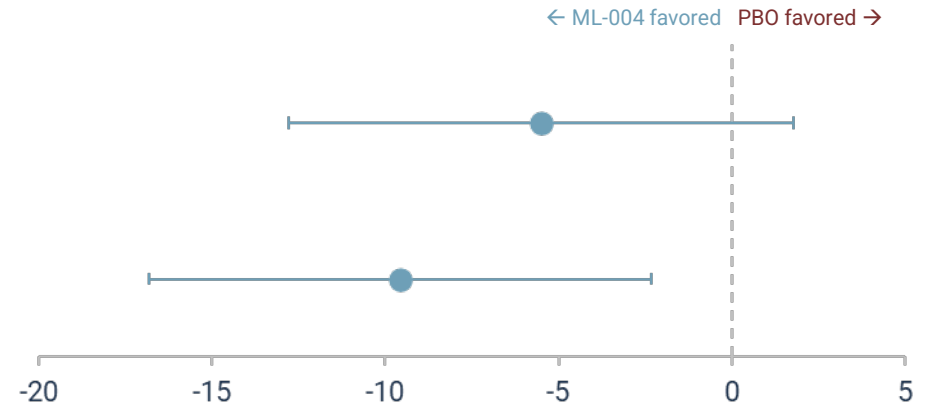
LS = least squares.
Note: Negative treatment deltas favor active treatment; effect size presented as an absolute value. Full Analysis set (FAS): The FAS includes all randomized subjects who received at least 1 dose of study drug after randomization and have DB Baseline and at least 1 post-DB Baseline assessment.

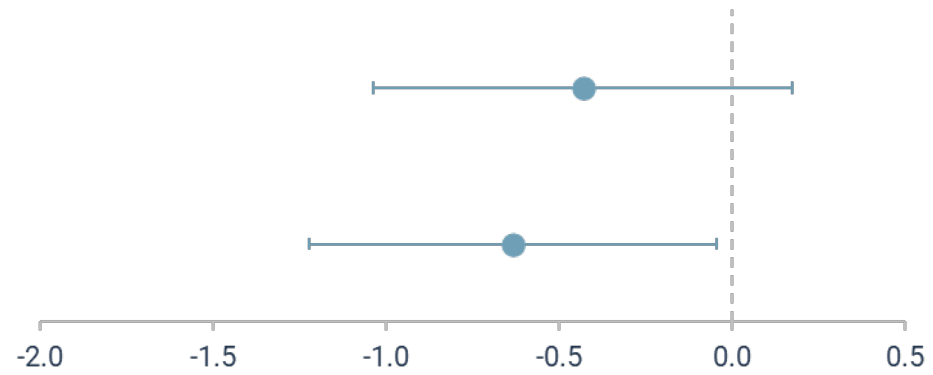
Irritability Outcomes

Includes Subjects with ABC-I ≥16 at Baseline

Two measures of irritability assessed by different raters

LS Mean Difference vs. Placebo (95% CI), by Scale and Age Group





		LS Mean Diff. [95% CI]	Effect Size	P-value (* $p < 0.05$)
ABC-I Subscale (1) *Care partner-reported*	Total N = 26	-5.5 [-12.8, 1.8]	0.64	0.131
	Adolescent N = 20	-9.6 [-16.8, -2.3]	1.33	**0.013 ***
CGI-I Irritability Domain (2) *Clinician-reported*	Total N = 26	-0.4 [-1.0, 0.2]	0.61	0.153
	Adolescent N = 20	-0.6 [-1.2, -0.0]	1.08	**0.036 ***

Note: Negative treatment deltas favor active treatment; effect size presented as an absolute value. Full Analysis set (FAS): The FAS includes all randomized subjects who received at least 1 dose of study drug after randomization and have DB Baseline and at least 1 post-DB Baseline assessment.

(1) ABC-I in the whole population was a key secondary endpoint evaluated in IRIS study; evaluation of change in the adolescent population was a prespecified endpoint

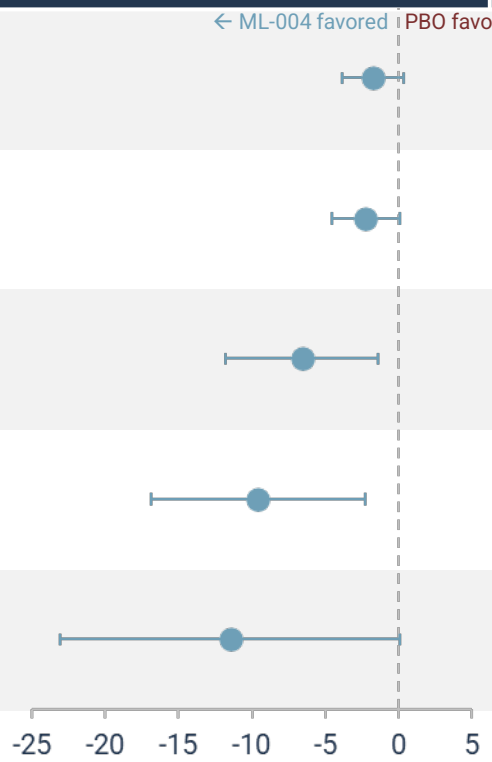
(2) CGI-I Global is included in labels for approved therapies.

Change From Baseline to End of Maintenance Dose

Adolescent Subgroup Analysis by Irritability Score at Baseline

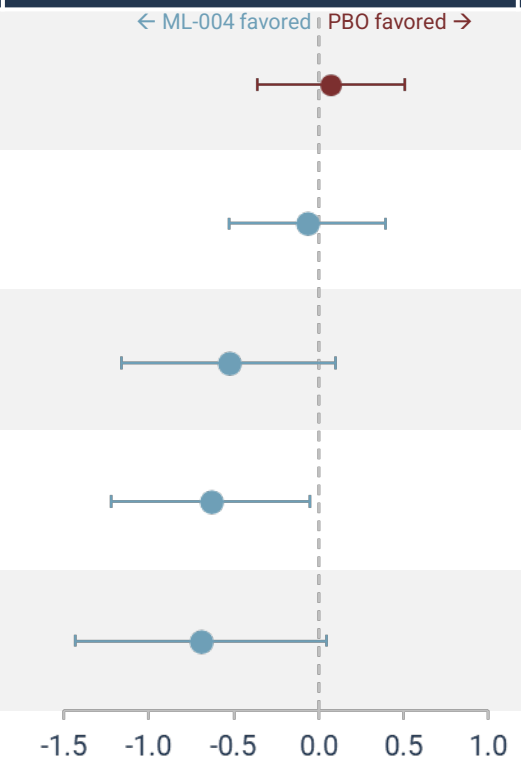
ABC-I Subscale

Subgroup N=active/PBO	LS Mean Diff [95% CI]	Effect Size	P-value (* p < 0.05)
All adolescents N = 49/51		0.34	0.107
ABC-I > 0 N = 43/48		0.43	0.054
ABC-I ≥ 13 N = 17/15		0.97	0.015 *
ABC-I ≥ 16 N = 11/9		1.33	0.013 *
ABC-I ≥ 18 N = 9/6		1.33	0.052



CGI-I Irritability Domain

Subgroup N=active/PBO	LS Mean Diff [95% CI]	Effect Size	P-value (* p < 0.05)
All adolescents N = 50/51		0.07	0.731
ABC-I > 0 N = 43/48		0.07	0.768
ABC-I ≥ 13 N = 17/15		0.64	0.097
ABC-I ≥ 16 N = 11/9		1.08	0.036 *
ABC-I ≥ 18 N = 9/6		1.16	0.065



Note: Negative treatment deltas favor active treatment; effect size presented as an absolute value. Full Analysis set (FAS): The FAS includes all randomized subjects who received at least 1 dose of study drug after randomization and have DB Baseline and at least 1 post-DB Baseline assessment.

ML-004 Was Generally Well Tolerated Across All Doses and Age Groups

Overview of Safety Observations

- Majority of TEAEs were mild, transient, and resolved without the need for dose reduction
- No severe or serious TEAEs occurred with ML-004 (all in PBO arm)
- No deaths or life-threatening events occurred
- Most frequent TEAEs (≥5% and >PBO) with ML-004 were headache, nausea, somnolence, vomiting, fatigue, and dizziness
- Adolescents experienced fewer TEAEs than adults, both overall and across common events
  - Adolescents: 62.7% for ML-004 vs. 41.2% for PBO
  - Adults: 86.7% for ML-004 vs. 72.4% for PBO
- Two adolescents discontinued (3.9%) due to a TEAE vs. 0% PBO
- Events commonly associated with commercial zolmitriptan [1] (e.g., jaw or chest pressure/tightening and paresthesia), were rare (N=1 each)

ML-004 Safety Profile

*Placebo-adjusted	Adolescents Treated with ML-004 (N=51)
Weight Gain	Mean ML-004 weight change less than PBO *+1.1kg vs. +1.9kg* [2]
Fatigue	1.9%*
Somnolence	11.8%*
Headache	9.8%*
EPS / Akathisia	Not Observed
Hyperprolactinemia / Endocrine	Not Expected
GI Effects	Nausea 9.8%*; Vomiting 5.9%*

TEAE = treatment-emergent adverse event in double-blind period.

(1) ZOMIG (zolmitriptan) U.S. Prescribing Information (2018).

(2) Based on adolescent weight changes observed between the double-blind baseline and Week 12

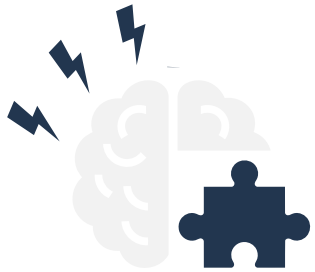
Unmet Medical Need

Chris Kroeger, M.D. | Co-Founder and Chief Executive Officer

Unmet Need in ASD Irritability Remains High

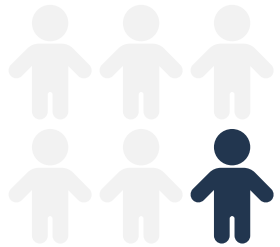
~830K

adolescents diagnosed with ASD (U.S., 2039E) (1)



~20-35%+

experience clinically significant irritability or aggression (2)



1 in 6

young people with ASD receive antipsychotics (3)

Only 2

approved therapies both with warnings and precautions relevant to adolescents

Incomplete Treatment Response

Additional options are needed to improve responses across a heterogeneous population

Meaningful Side-Effect Burden

Weight gain, sedation and movement-related effects may impair daily functioning

Challenges with Long-Term Use

Tolerability concerns may limit chronic treatment, particularly in younger populations

Caregiver Hesitancy

Safety concerns may discourage treatment, particularly in younger patients without psychosis

(1) *2039 projection of U.S. adolescents; 2022 NSCH and Grosvenor et al., 2023 claims data.*
(2) *Alatrash et al., 2024; Manter et al., BMC Medicine 2025.*
(3) *Park et al., JAACAP 2016 meta-analysis.*

Current Standard of Care in ASD Irritability

	Risperidone	Aripiprazole
Effect Size (ABC-I)	0.92 - 1.2	0.43 - 0.87
Weight Gain	**Adverse events** • Weight increased 6% (1) • Increased appetite 29% (1) **Weight change** • 1.4 kg more weight gain (2) • 26% more subjects gained ≥7% weight (2)	**Adverse events** • Decreased appetite 5% (1) **Weight change** • 1.2 kg greater weight gain (3) • 19% more subjects gained ≥ 7% weight (3)
Fatigue/Somnolence	• Fatigue 22% (1) • Sedation 48% (1)	• Fatigue 15% (1) • Lethargy 5% (1) • Somnolence 6% (1) • Sedation 17% (1)
EPS / Akathisia / Tardive Dyskinesia	• Parkinsonism 7% (1) • Tremor 7% (1)	• EPD 6% (1) • Tremor 10% (1)
Hyperprolactinemia / Endocrine	• Elevated Prolactin 47% (4) • Gynecomastia 2.3% (4)	• No adverse events reported in autism
Cardiovascular	• Warning for Orthostatic Hypotension • HR increased 1.9 bpm(3)	• Warning for Orthostatic Hypotension
GI Effects	• Constipation 11% (1) • Nausea 3% (1) • Vomiting 3% (1) • Drooling 8% (1)	• Vomiting 7% (1) • Drooling 9% (1)

Meaningful side-effect burden offers a compelling opportunity for better-tolerated treatment options

Sources: RISPERDAL® prescribing information, revised 2025; ABILIFY® prescribing information, revised 2025.

(1) PBO-adjusted double-blind short-term trials in autism, TEAE > 5% table.

(2) PBO-adjusted, pediatric patients (5 to 17 years) with schizophrenia, bipolar disorder, autistic disorder, or other psychiatric disorders. In short-term trials (3 to 8 weeks).

(3) PBO-adjusted, trials in autism (8-week duration).

(4) PBO-adjusted, 8-week trial in children and adolescents (5 to 17 years) with autistic disorder or psychiatric disorders.

ML-004 Has the Potential to Address Unmet Needs Through Established Development Path

Potential Differentiation with ML-004

Initial efficacy signal from IRIS appears in line with approved therapies (1)

- ✓ Clinically meaningful improvement observed across ABC-I and CGI-I in adolescents with elevated irritability
- ✓ Magnitude of effect appears comparable to approved therapies, based on cross-trial comparisons

Potential for differentiated tolerability profile

- ✓ No signal for weight gain or EPS; low rates of somnolence, particularly among adolescents
- ✓ Most AEs were mild and transient, with no severe or serious AEs with ML-004

5-$HT_1B/_1D$ agonism may offer patients and caregivers an alternative approach to current D_2-based therapies

Historical Development Precedents (2)

- **Efficient trial designs supported prior approvals**
  - Pivotal studies were 8 weeks and generally enrolled approximately 100 patients
- **Focused clinical programs**
  - Studies generally conducted in the U.S. across a limited number of sites (3)
- **Established regulatory endpoint**
  - ABC-I served as the primary efficacy endpoint supporting prior approvals

(1) *Cross-trial comparisons are inherently limited due to differences in study design, patient populations and analytical methods.*
(2) *RISPERDAL® prescribing information, revised 2025; ABILIFY® prescribing information, revised 2025.*
(3) *Based on publicly disclosed study designs of RISPERDAL® and ABILIFY® for irritability associated with ASD.*

Closing Remarks

Chris Kroeger, M.D. | Co-Founder and Chief Executive Officer

Closing Remarks

01 ML-004 demonstrated clinically meaningful improvements in irritability in adolescents with moderate or greater baseline irritability across both caregiver- and clinician-rated scales

- ABC-I (effect size of 1.33, nominal p-value of 0.013)
- CGI-I irritability (effect size of 1.08, nominal p-value of 0.036)

02 ML-004 was generally well tolerated across all doses and age groups

- No drug-related severe or serious AEs
- Meaningful differentiation from standard of care atypical antipsychotics
  - No weight gain relative to placebo
  - No evidence of extrapyramidal symptoms
  - Low rates of fatigue / somnolence

Data support potential development of ML-004 for irritability associated with ASD, an indication with high unmet need and an established regulatory path; next steps will be guided by upcoming regulatory interactions

Advancing a Broad and Diversified Pipeline

Program	Circuit	Indications	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
ML-007C-MA M_1/M_4 agonist co-formulated with PAC	Direct and Indirect Pathways	Schizophrenia			ZEPHYR		**Topline results by mid-August 2026**
		Alzheimer's Disease Psychosis		Fast Track	VISTA		Topline results in 2H 2027
ML-004 5-$HT_{1B/1D}$ agonist	Dorsal Raphe to Nucleus Accumbens	Autism Spectrum Disorder Sociability/Irritability			IRIS		**Engage with FDA at EOP2 meeting**
ML-009 GPR52 PAM	Indirect Pathway	Hyperactivity/Impulsivity					Complete IND-enabling studies in 2027
ML-055 Next-Gen M_1/M_4 agonist	Direct and Indirect Pathways	Neuropsychiatric Disorders					Nominate preclinical candidate in 2026
ML-021 M_4 antagonist	Direct Pathway	Parkinson's Disease					Finalize preclinical candidate in 2027

Potential in other indications being explored

Leveraging our versatile circuit-based discovery platform for ongoing pipeline expansion

GPR = G-protein-coupled receptor. PAC = peripherally acting anti-cholinergic. PAM = positive allosteric modulator.

MapLight

MapLight

Q&A