Slate Medicines Corporate Overview

August 17, 2026

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Important Additional Information About the Proposed Merger Will be Filed with the SEC

This Presentation is not a substitute for the registration statement or for any other document that Fulcrum may file with the SEC in connection with the proposed merger. In connection with the proposed merger between Fulcrum and the Company, Fulcrum intends to file relevant materials with the SEC, including a registration statement on Form S-4 that will contain a proxy statement/prospectus of Fulcrum. FULCRUM URGES INVESTORS AND STOCKHOLDERS TO READ THE REGISTRATION STATEMENT, PROXY STATEMENT/PROSPECTUS AND ANY OTHER RELEVANT DOCUMENTS THAT MAY BE FILED WITH THE SEC, AS WELL AS ANY AMENDMENTS OR SUPPLEMENTS TO THESE DOCUMENTS, CAREFULLY AND IN THEIR ENTIRETY IF AND WHEN THEY BECOME AVAILABLE BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION ABOUT FULCRUM, THE COMPANY, THE PROPOSED MERGER AND RELATED MATTERS. Investors and stockholders will be able to obtain free copies of the proxy statement/prospectus and other documents filed by Fulcrum with the SEC (when they become available) through the website maintained by the SEC at www.sec.gov. Stockholders are urged to read the proxy statement/prospectus and the other relevant materials when they become available before making any voting or investment decision with respect to the proposed merger. In addition, investors and stockholders should note that Fulcrum communicates with investors and the public using its website (ir.fulcrumtx.com).

Participants in the Solicitation

Fulcrum, the Company and their respective directors and executive officers may be deemed to be participants in the solicitation of proxies from stockholders in connection with the proposed merger. Information about Fulcrum's directors and executive officers, including a description of their interests in Fulcrum, is included in Fulcrum's definitive proxy statement on Schedule 14A for its 2026 Annual Meeting of Stockholders as filed with the SEC, and in filings by such individuals on Form 4. Additional information regarding these persons and their interests in the transaction will be included in the proxy statement/prospectus relating to the proposed merger when it is filed with the SEC. These documents can be obtained free of charge from the sources indicated above.

Fulcrum Therapeutics announces merger with Slate Medicines

Overview	• Stock-for-stock merger whereby all of Slate Medicine's issued and outstanding capital stock will be exchanged for Fulcrum common stock • Concurrent $245 million private placement into Slate from a syndicate of leading healthcare investors led by Frazier Life Sciences, with participation from Forbion, RA Capital Management, Deep Track Capital, Foresite Capital, OrbiMed, RTW Investments, and Mingxin Capital. • Prior to the closing of the merger, Fulcrum expects to declare a cash dividend to the pre-merger Fulcrum stockholders equal to the amount by which Fulcrum's net cash exceeds $20.3 million • Estimated pro forma ownership split: Fulcrum: 5.0%, Slate: 55.9%, Private Placement Investors: 39.1%
Use of Proceeds	• To support the advancement of SLTE-1009 through a Phase 1 healthy volunteer study and a Phase 2 dose-range finding study in migraine patients as well as advancement of Slate's pipeline. • Pro forma cash balance at closing is anticipated to fund Slate's current planned operations into 2029.
Management and Board	• The combined company will operate as Slate Medicines, Inc. and be led by Gregory Oakes, Chief Executive Officer. • Slate's Board of Directors is expected to serve as the board for the combined company.
Timing	• Merger and financing expected to close in Q4 2026

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Slate Medicines is a biotech company advancing next-generation therapeutics for migraine

The Opportunity

Migraine is a prevalent, debilitating neurological disease, and many patients are underserved with existing therapies

Migraine is the leading cause of disability in people under the age of 50[1] and existing treatment options do not provide millions of patients with complete control of their disease

The Science

PACAP (pituitary adenylate cyclase-activating polypeptide) and VIP (vasoactive intestinal peptide) play a foundational role in migraine pathophysiology

PACAP-ligand blockade is a clinically validated approach in the prevention of migraines

The Solution

SLTE-1009 is a potentially differentiated subcutaneous anti-PACAP/VIP monoclonal antibody for the prevention of migraine and other headache disorders

Slate is committed to understanding and innovating in the biology of migraine to better address the disease

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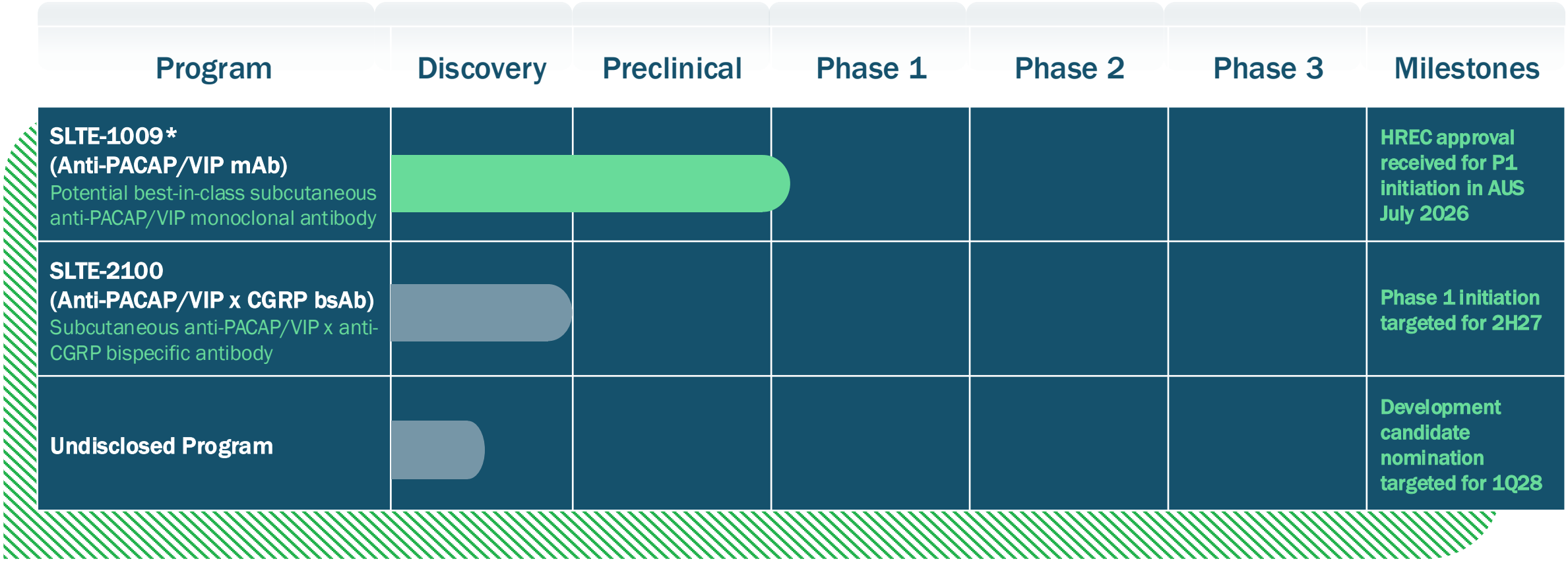
1. Timothy J Steiner et al., "Migraine Is First Cause of Disability in under 50s: Will Health Politicians Now Take Notice?," The journal of headache and pain, February 21, 2018, https://pmc.ncbi.nlm.nih.gov/articles/PMC5821623/#:~:text=With%20better%20knowledge,%20empirical%20data,7.2%25)%20(Table%201)
2. "Migraine and Other Headache Disorders," World Health Organization, n.d., https://www.who.int/news-room/fact-sheets/detail/headache-disorders.

Slate Medicines is seeking to broaden the treatment paradigm for migraine



*Slate licensed the ex-China development and commercialization rights for SLTE-1009 from DartsBio Pharmaceuticals (Guangdong), Ltd

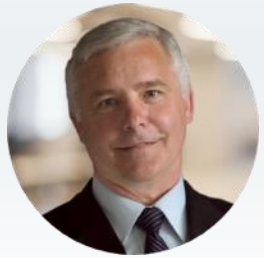
mAb = monoclonal antibody
HREC = Human Research Ethics Committee
CGRP = calcitonin gene-related peptide
bsAb = bispecific antibody

Led by a team of experienced biopharma executives with a personal commitment to migraine

Executive Team

Gregory Oakes, MBA
Chief Executive Officer

Neil Buckley, MS
President and Chief Operating Officer

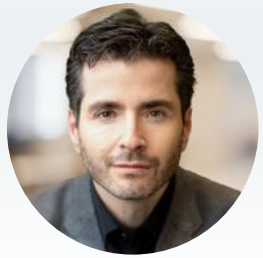


Roger Cady, MD
Chief Medical Officer

John Umstead, CPA
Chief Financial Officer

Board Of Directors

Gregory Oakes, MBA
Chief Executive Officer



Peter Kolchinsky, PhD
Managing Partner, RA Capital

Tim Lohoff, PhD
Principal, Forbion

Michael Rome, PhD
Managing Director, Foresite Capital

Mark W. Hahn

Raised $130 million Series A; backed by top-tier investors

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Migraine patients are underserved by the existing standard of care

Migraine is more than just a headache; it is one of the most prevalent, lifelong, and disabling neurological diseases

Migraine is the leading cause of disability in people under the age of 50[1]

Migraine is often a lifelong disease that affects people of all ages; Headache disorders are among the top three most common neurological conditions ages 5-80[2]

Migraine affects women about 2–3 times more often than men, especially during reproductive years[3]

The disability caused by migraine is far broader than just headache and comprises several phases and a spectrum of disabling symptoms, all of which can significantly impact a person's ability to function

Symptoms of migraine include moderate to severe throbbing and pulsating pain on one side of the head, migraine aura, nausea, vomiting, flushing, dizziness, difficulty focusing, and light sensitivity

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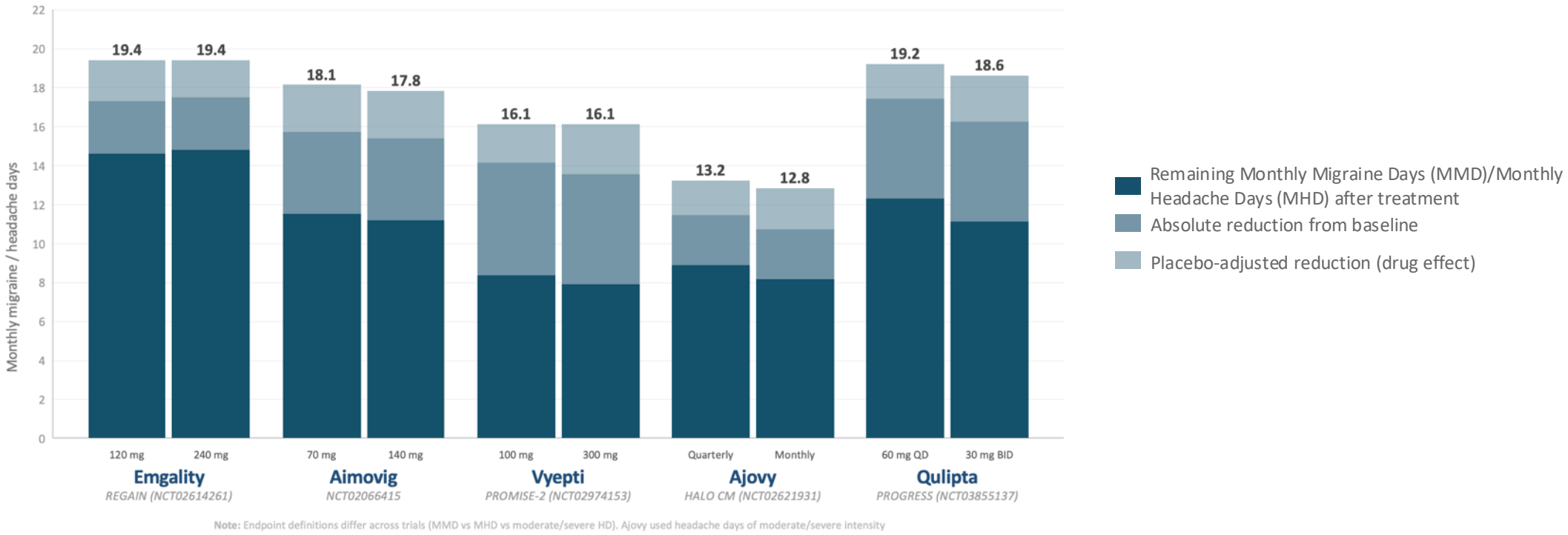
1. Timothy J Steiner et al., "Migraine Is First Cause of Disability in under 50s: Will Health Politicians Now Take Notice?," The journal of headache and pain, February 21, 2018,
2. "Migraine and Other Headache Disorders," World Health Organization, n.d., https://www.who.int/news-room/fact-sheets/detail/headache-disorders.
3. Rosse, et. al. Sex and gender differences in migraines: a narrative review Neurol Sci. 2022 Sep;43(9):5729-5734. doi: 10.1007/s10072-022-06178-6. Epub 2022 Jun 8.

Existing preventative therapeutics, including CGRP antagonists, do not provide complete disease control for most patients

- In pivotal studies in chronic migraine (CM) patients, only ~50% of patients experience a >50% reduction in monthly migraine or headache days, and only ~20% of patients experience a >75% reduction
- American Headache Society clinical guidelines state patients experiencing ≥4 migraine days per month should be offered preventative treatment



Note: Endpoint definitions differ across trials (MMD vs MHD vs moderate/severe HD). Ajovy used headache days of moderate/severe intensity

1. https://d1fakw34cbtrm5.cloudfront.net/PDFs/Migraine-Quick-Guides/AHS-First-Contact-PreventativeTreatment.pdf
2. **REGAIN (NCT02614261)** — Detke et al. Galcanezumab in chronic migraine: The randomized, double-blind, placebo-controlled REGAIN study. *Neurology*. 2018;91(24):e2211–e2221.
3. **NCT02066415** — Tepper et al. Safety and efficacy of erenumab for preventive treatment of chronic migraine: a randomised, double-blind, placebo-controlled phase 2 trial. *Lancet Neurology*. 2017;16(6):425–434.
4. **PROMISE-2 (NCT02974153)** — Lipton et al. Efficacy and safety of eptinezumab in patients with chronic migraine: PROMISE-2. *Neurology*. 2020;94(13):e1365–e1377.
5. **HALO CM (NCT02621931)** — Silberstein et al. Fremanezumab for the preventive treatment of chronic migraine. *New England Journal of Medicine*. 2017;377(22):2113–2122.
6. **PROGRESS (NCT03855137)** — Pozo-Rosich et al. Atogepant for the preventive treatment of chronic migraine (PROGRESS): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2023;402(10404):775–785.

Despite modest efficacy, CGRP antagonists for prevention are a large and growing commercial market

Company	Drug	Modality	Dosing frequency	2025 Sales
Pfizer	Nurtec ODT (rimegepant) orally disintegrating tablets 75 mg	Small molecule	QOD	**$1,424M*** (Pfizer 2025 annual report)
abbvie	QULIPTA (atogepant) tablets	Small molecule	QD	**$1,036M** (Abbvie 2025 8-K)
Lilly	Emgality (galcanezumab-gnlm) 120 mg injection	Subcutaneous antibody	QM	**~$700M (est)** (Estimate from Q3 Zack's Report)
Lundbeck	Vyepti (eptinezumab-jjmr) 100 mg/mL Injection for IV	Intravenous antibody	Q3M	**$700M** (DKK 4,476M) (Lundbeck FY2025 Corporate Release)
teva	AJOVY (fremanezumab-vfrm) injection 225 mg/1.5 mL	Subcutaneous antibody	QM/Q3M	**$673M** (Teva FY2025 press release)
AMGEN NOVARTIS	Aimovig (erenumab-aooe) injection 70 mg/mL • 140 mg/mL	Subcutaneous antibody	QM	**~$500M (est)** (Novartis Form 6-K FY2025) (Amgen 3Q 25 8-K other products estimate)

In 2025, CGRP antagonists for migraine prevention **sold approximately $5 billion** and are expected to reach peak class sales of **$12.5 billion in 2033***

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*includes gepants for acute use

QOD = every other day; QD = every day, QM – every month, Q3M = every 3 months

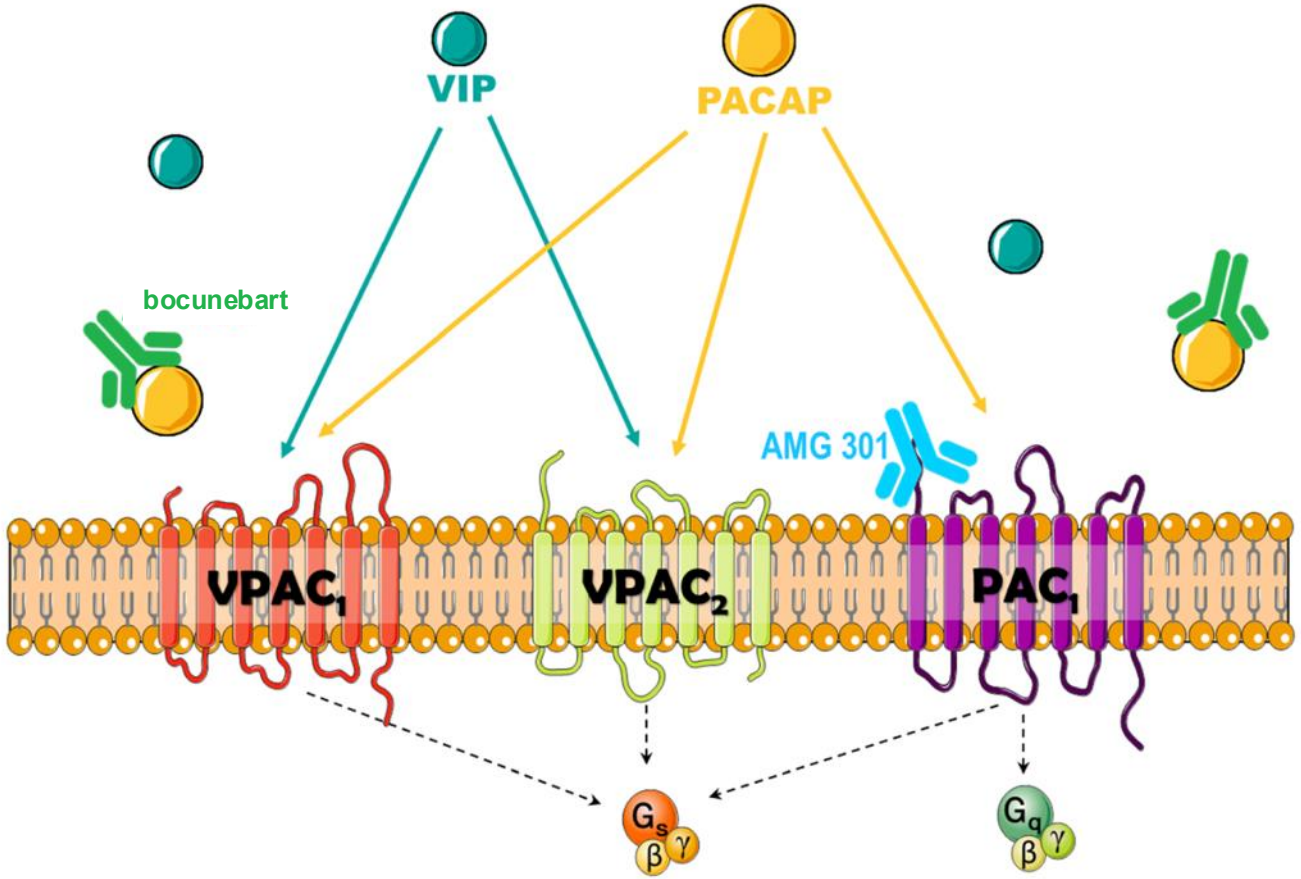
Persistence Market Research. "CGRP Inhibitors Market Size, Share, and Growth Forecast 2026–2033." Report ID: PMRREP33710. February 2026. 199 pages. Available at: https://www.persistencemarketresearch.com/market-research/cgrp-inhibitors-market.asp

PACAP and VIP play a foundational role in migraine pathophysiology

PACAP and VIP are neuropeptides that signal through multiple receptors and ligand blockade is required for efficacy

PACAP exists in two isoforms: PACAP-38 and PACAP-27

VIP is a neuropeptide that shares 68% sequence homology with PACAP and signals through common receptors, VPAC1 and VPAC2



- **AMG301**, a PAC1 receptor binding antibody, failed to show a statistically significant benefit over placebo in a Phase 2 migraine prevention study,
- **Bocunebart (Lu AG09222)** is a ligand-binding antibody that prevents PACAP-38 and PACAP-27 interaction with PAC1, VPAC1, and VPAC2, and has shown encouraging efficacy in randomized and controlled clinical trials

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Image: Rubio-Beltrán et al. The Journal of Headache and Pain (2018) 19:64 https://doi.org/10.1186/s10194-018-0893-8
AMG301 - NCT03238781

Like CGRP, PACAP and VIP have each been shown to independently induce migraine-like headaches

PACAP, VIP, and CGRP are all neuropeptides and have been shown to induce cephalic vasodilation and the induction of migraine-like headache in patients

Neuropeptide	Migraine induction rate	Notes
CGRP	**63%**	• 20-minute IV infusion • Median time to onset of migraine 3 hours • 9% premonitory symptoms
PACAP-38	**72%**	• 20-minute IV infusion • Median time to onset of migraine 5 hours • 48% of patients experienced premonitory symptoms
VIP	**71%**	• 2-hour IV infusion ○ 20-minute infusions of VIP do not induce migraine as with PACAP and CGRP • Mimicked a spontaneous migraine attack

PACAP-38 and VIP each independently produce migraine-like headache in patients at high rates, each with a unique clinical signature

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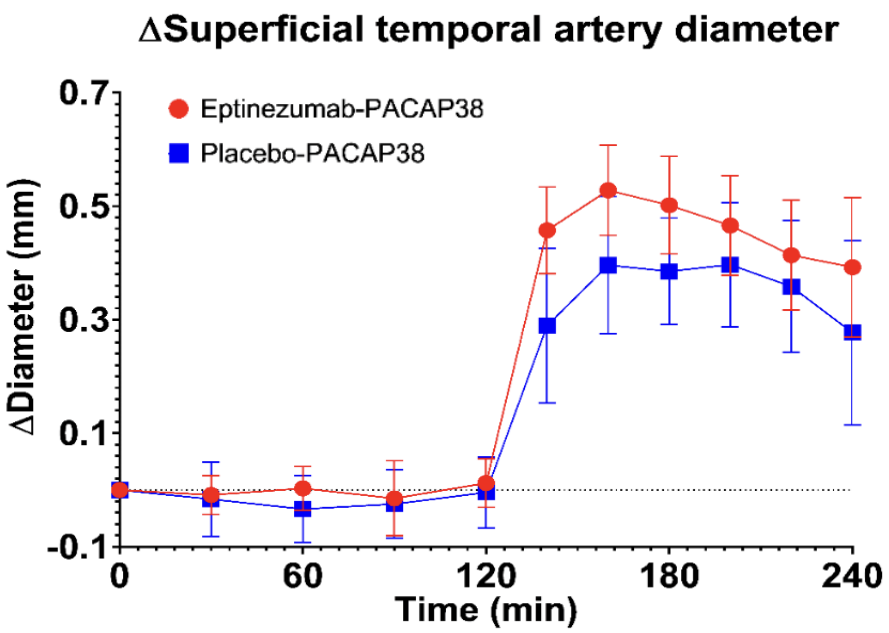
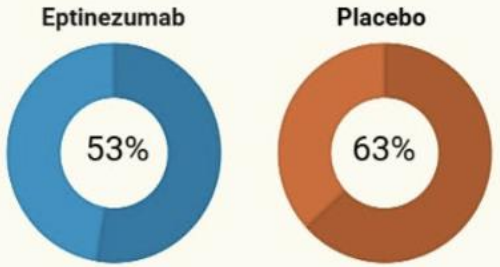
1. Guo S, et al. Premonitory and nonheadache symptoms induced by CGRP and PACAP38 in patients with migraine. Pain. 2016 Dec;157(12):2773-2781. doi: 10.1097/j.pain.0000000000000702.
2. Pellesi L, et al. Effect of Vasoactive Intestinal Polypeptide on Development of Migraine Headaches: A Randomized Clinical Trial. JAMANetw Open. 2021 Aug 2;4(8):e2118543. doi: 10.1001/jamanetworkopen.2021.18543

Challenge studies have demonstrated that PACAP induces migraine independent of CGRP signaling



RESULTS

There was no difference in incidence of PACAP-38-induced migraine attacks between the two groups ($P = 0.74$).



We found no differences in incidence of headache induction ($P > 0.99$), or area under the curve for headache intensity scores ($P = 0.96$).

CONCLUSION

PACAP-38 can mediate its signaling independently of CGRP signaling in migraine pathogenesis, indicating that therapies targeting PACAP signaling are a promising new avenue for treating migraine.

In a randomized and controlled PACAP-38 challenge study, anti-CGRP treatment did not prevent migraine induction by PACAP-38, indicating **PACAP is an orthogonal driver of migraine to CGRP**

- Patients were randomized to receive either placebo or anti-CGRP monoclonal antibody eptinezumab (Vyepti) and then infused with PACAP-38 start at 120 minutes
- There was no meaningful difference in physiologic parameters tested, including superficial temporal artery diameter, facial skin blood flow, mean arterial blood pressure, or heart rate
- There was no statistical difference in migraine induction rates between the pre-treated and placebo group

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Al-Karagholi et al. *PACAP38-induced migraine attacks are independent of CGRP signaling: a randomized controlled trial,* The Journal of Headache and Pain https://doi.org/10.1186/s10194-025-02022-2 (2025)

PACAP-ligand binding is a clinically-validated approach to migraine prevention

- **In the Phase 2a HOPE study, bocunebart (Lu AG09222), an anti-PACAP IV ligand binding mAb, demonstrated a significant monthly migraine reduction in high frequency, treatment experienced chronic migraine**
  - Patients in HOPE had baseline average MMD of 16.7 and all had failed 2-4 preventative therapeutics
- **In June 2026, Lundbeck presented data from the Phase 2b PROCEED trial demonstrating a statistically significant reduction in a pooled episodic and chronic migraine study with IV administration**
  - The subcutaneous portion of the study was discontinued in March 2025 after a planned interim futility analysis
  - Utilized a pooled analysis of HOPE and PROCEED bocunebart demonstrated a -2.3-placebo adjusted MMD reduction in chronic migraine
  - Dose A met statistical significance with a -1.4-placebo adjusted MMD reduction in a pooled episodic and chronic population

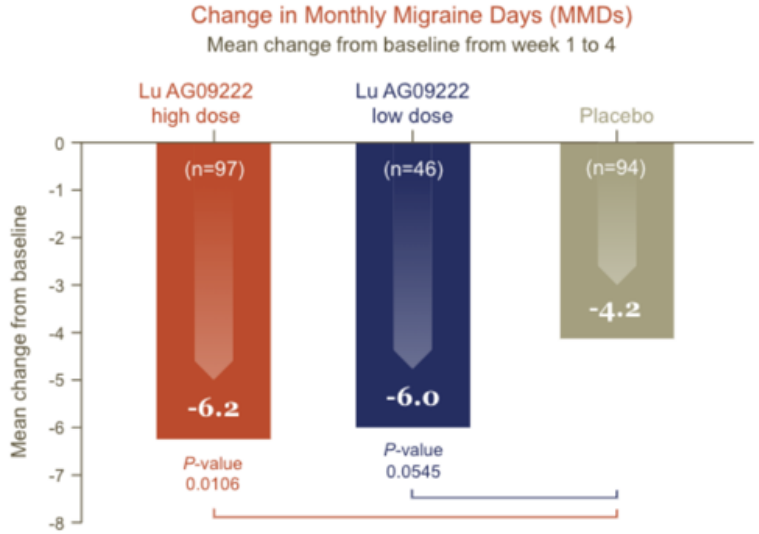
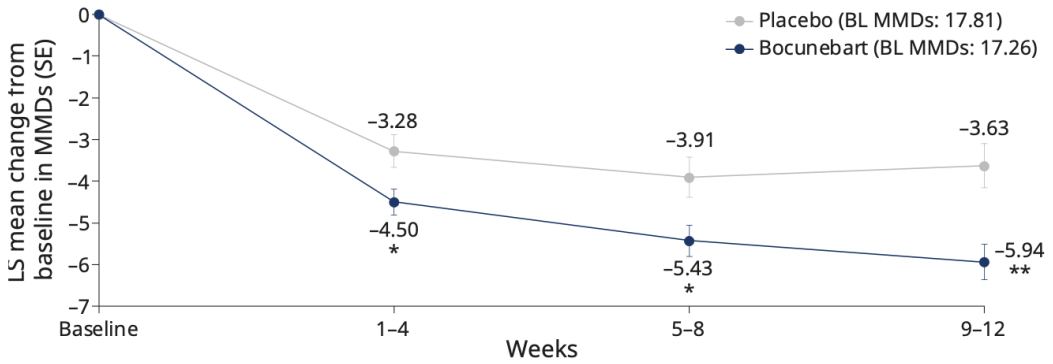


Figure 2. Change from baseline in MMDs in participants with CM

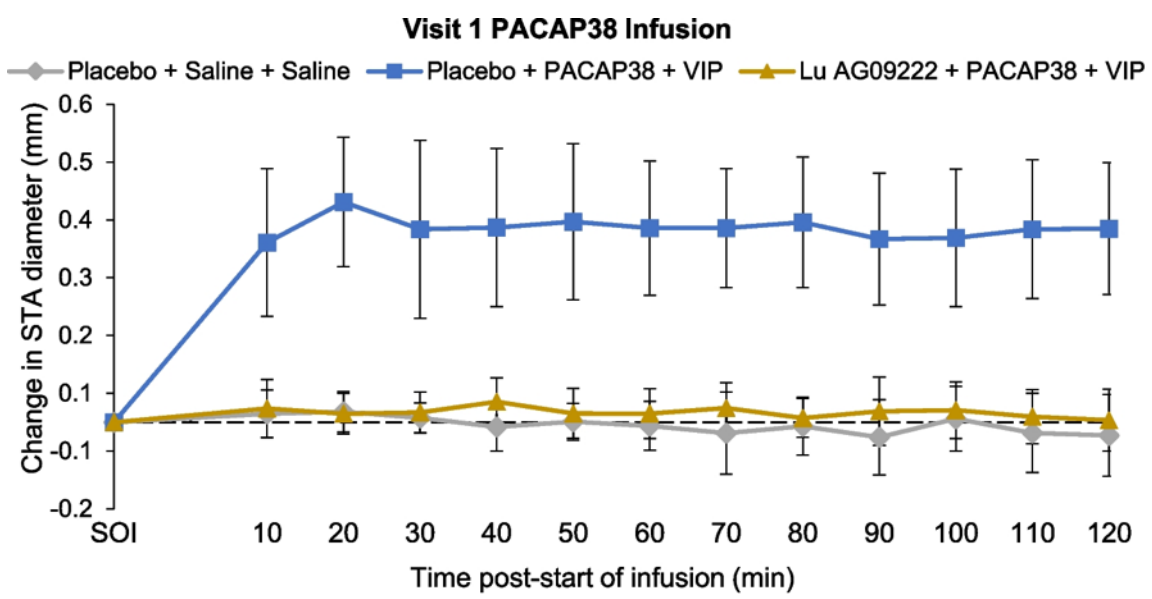


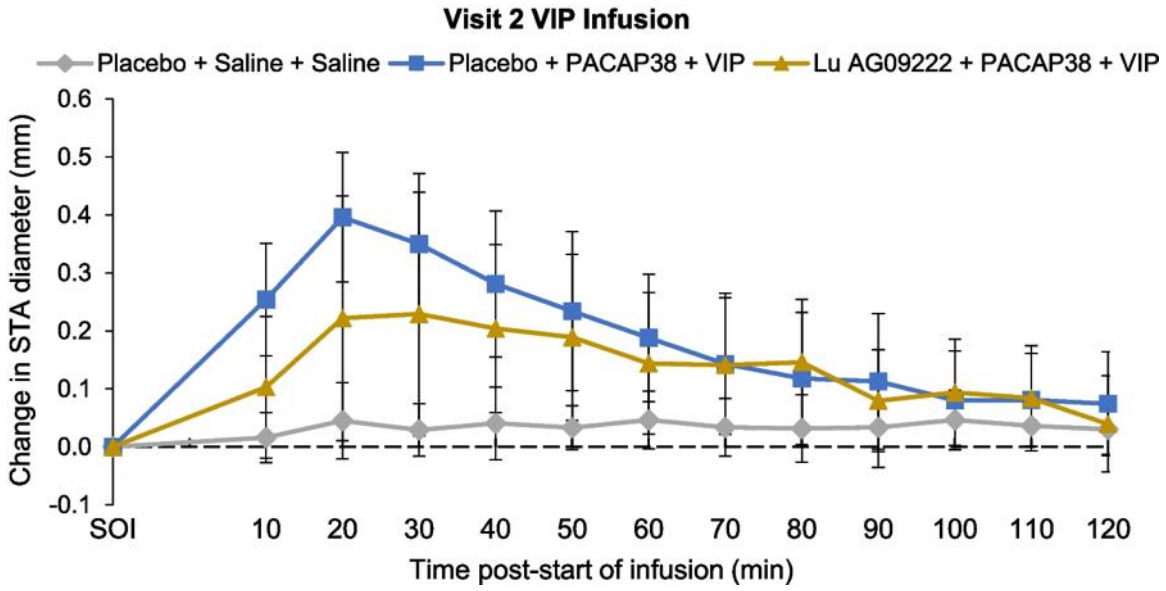
Bocunebart n=	354	217	182
Placebo n=	214	130	113

PROCEED+HOPE, FAS, MMRM: Pooled data included all doses and routes of administration (IV and SC). Post-hoc analyses: *p<0.05 vs placebo; **p<0.001 vs placebo.

Ashina M, et al. A Monoclonal Antibody to PACAP for Migraine Prevention. *New England Journal of Medicine*. 2024;391(9). DOI: 10.1056/NEJMoa2314577
Allaini, et. Al., *Targeting PACAP in migraine prevention: Outcomes from the PROCEED phase 2b trial of bocunebart (Lu AG09222)* (2026)

Bocunebart demonstrated complete reversal of PACAP-associated vasodilation, but only partial reversal of VIP associated effects





In an infusion challenge study, bocunebart completely reversed PACAP-38 associated superficial temporal artery vasodilation, but only partially reverse the effects of VIP

Rasmussen et al. The effect of Lu AG09222 on PACAP38- and VIP-induced vasodilation, heart rate increase, and headache in healthy subjects: an interventional, randomized, double-blind, parallel-group, placebo-controlled study. The Journal of Headache and Pain (2023) 24:60 https://doi.org/10.1186/s10194-023-01599-w

SLTE-1009: A potential best-in-class subcutaneous anti-PACAP/VIP monoclonal antibody for the prevention of migraine

SLTE-1009: A potentially differentiated subcutaneous anti-PACAP/VIP monoclonal antibody for the prevention of migraine

Property	SLTE-1009	Bocunebart (Lu AG09222)
Ligand Binding	✓ Yes	✓ Yes
PACAP-38 and PACAP-27	✓ Yes	✓ Yes
VIP	✓ Yes	– Low affinity, partial affect
Half-life extended	✓ Yes - YTE	✗ No
Delivery and frequency	✓ Subcutaneous Monthly with the potential for Q3M	✗ Being developed intravenous Monthly

SLTE-1009 offers the potential for enhanced efficacy with enhanced VIP binding vs. PACAP-only targeting therapies and **improved delivery over bocunebart,** allowing for subcutaneous administration

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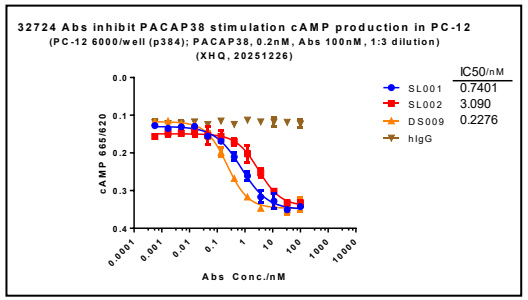
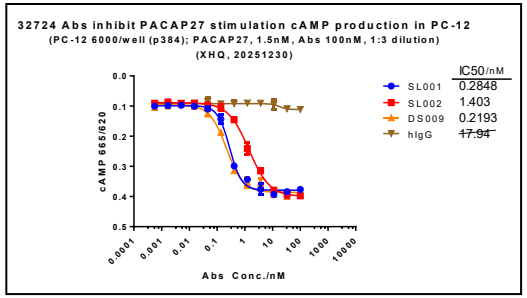
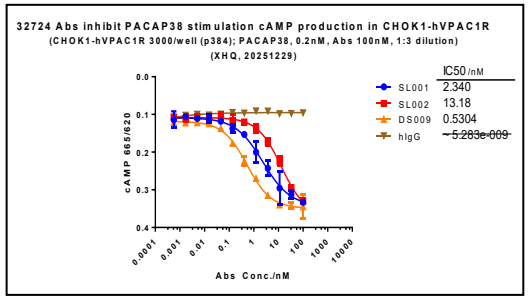
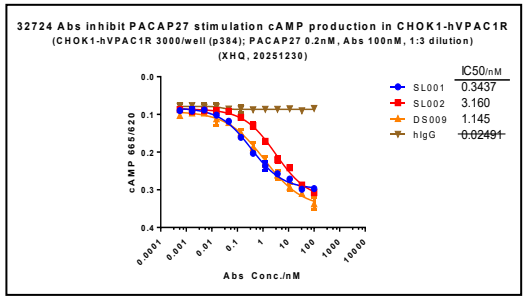
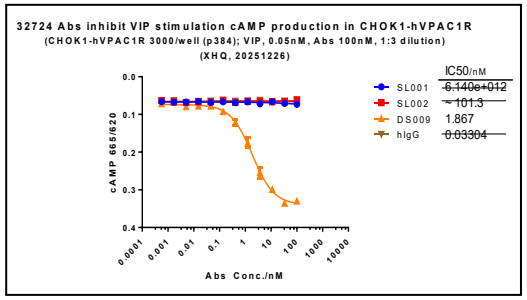
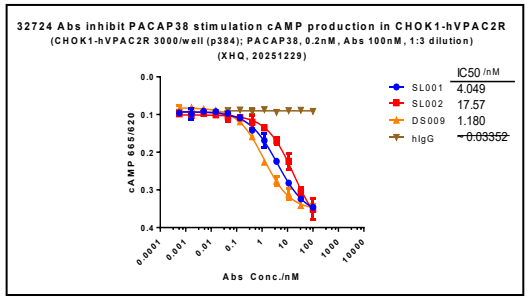
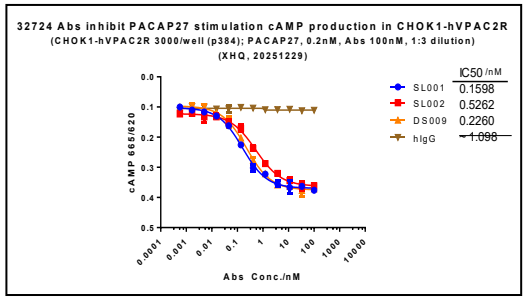
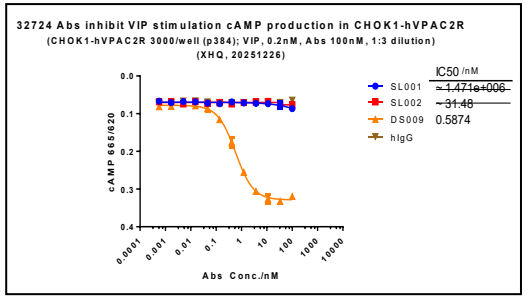
Internal Data
Ashina et. al Pharmacokinetics and safety of bocunebart (Lu AG09222), an anti-PACAP monoclonal antibody in development for migraine prevention, AAN 2026 Poster

In functional cellular assays SLTE-1009 demonstrated equivalent potency to bocunebart on PACAP and enhanced blockade of VIP

Activity	Antigen	SLTE-1009 IC(50)	Bocuenbart IC(50)
PAC1 neutralizing	*PACAP38*	0.23 nM	0.74 nM
	PACAP27	0.22 nM	0.29 nM
VPAC1 neutralizing	*PACAP38*	0.53 nM	2.34 nM
	PACAP27	1.15 nM	0.34 nM
	VIP	1.87 nM	NI*
VPAC2 neutralizing	*PACAP38*	1.18 nM	4.05 nM
	PACAP27	0.23 nM	0.16 nM
	VIP	0.59 nM	NI*

*High concentration of 100 nM in cell assays, SPR indicates bocunebart KD in this range

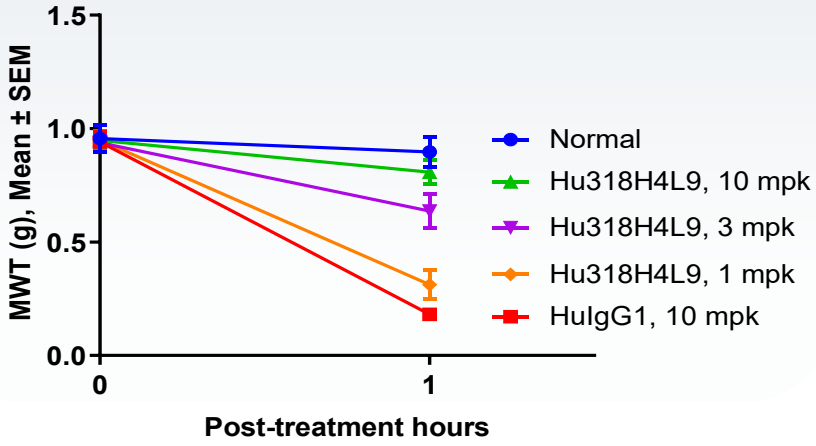
	PACAP38	PACAP27	VIP
PC-12 (PAC1R)			
CHOK1-VPAC1R			
CHOK1-VPAC2R			

Activity in preclinical models of migraine

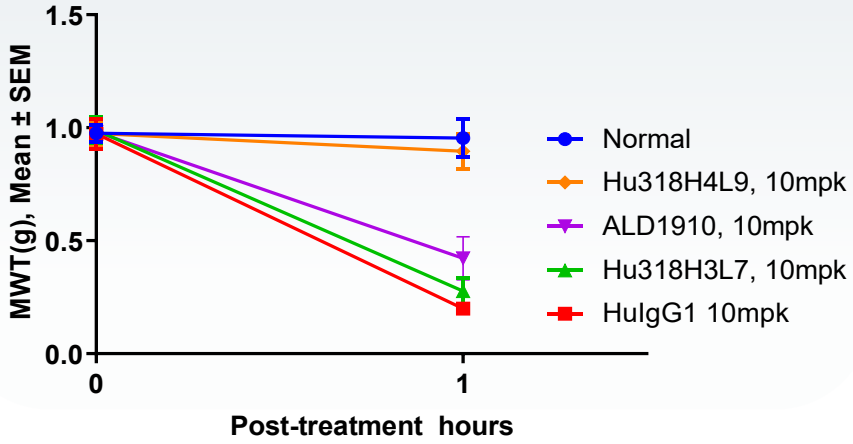
UMB: 12 μg
Female C57BL/6J
18-20 g, N = 8

Priming by Restrain stress → Baseline test Randomization → -50 min Treatments (i.v.) → Pain threshold test (1h)

UMB-induced mouse migraine pain threshold (Von Frey)
n = 8, i.v.



UMB-induced mouse migraine pain threshold (Von Frey)
n = 8, i.v., 10 mpk



Hu318H4L9 = SLTE-1009
ALD1910 = bocunebart (Lu AG09222)

- Umbellulone (UMB) is a naturally occurring, allodynia-inducing monoterpene ketone via activation of Transient receptor potential cation channel, subfamily A, member 1 (TRPA1)
- UMB-induced sensory hypersensitivity responses are associated with activation of the trigeminal neurovascular pathway
- SLTE-1009 showed dose dependent effects on allodynia and was superior to bocunebart head-to-head at 1 hour

SLATE MEDICINES

SLTE-1009 thus far has demonstrated favorable preclinical data

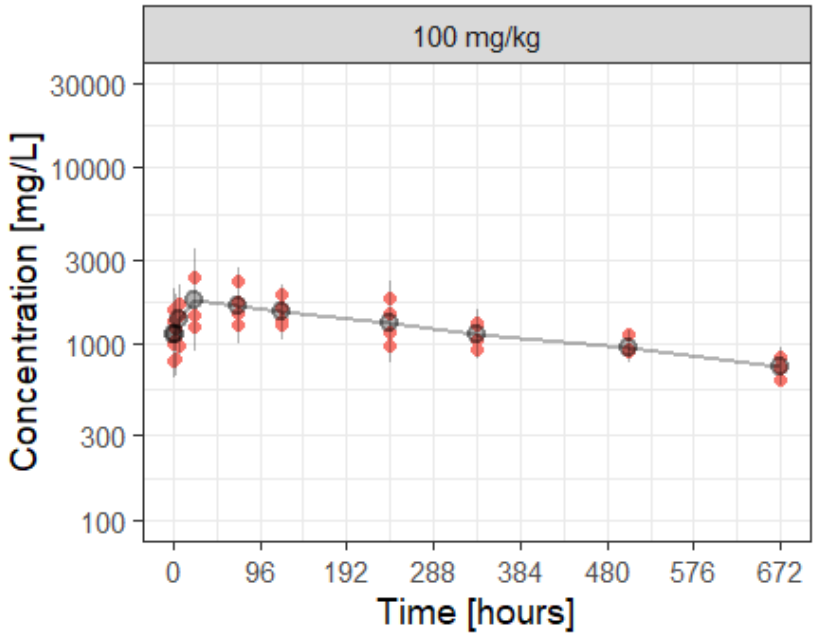
Formulation Product Profile

Property	Target	SLTE-1009
Concentration	≥150 mg/mL	✓
Viscosity	<15 cP	✓
Osmolality	<500 mSOM/kg	✓
Stability	Potency	✓
	Subvisible particles	✓
	Charge distribution	✓
	Aggregation	✓
Autoinjector compatible volume	Single ≤2 mL injection	✓

In addition to favorable CMC-related properties, the highest dose tested in both non-human primates (NHP) and rodent GLP toxicology studies was determined to be the no observed adverse effect level (NOAEL)

SLATE MEDICINES

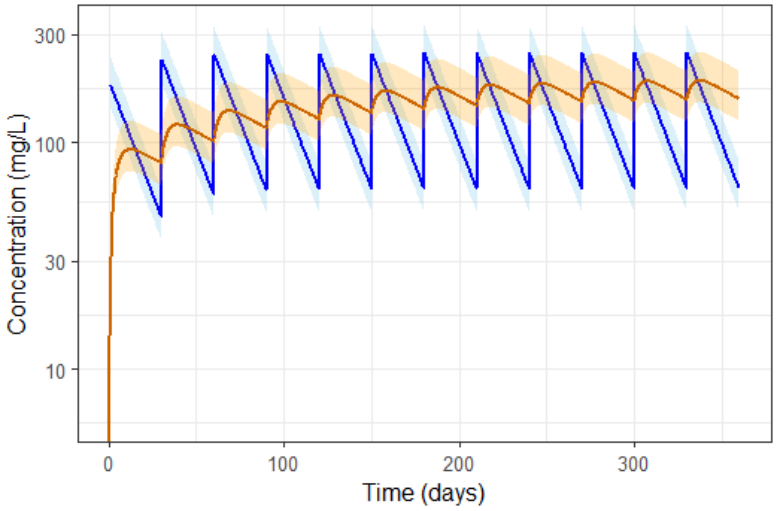
Demonstrated half-life extension in NHPs and ability to match Lundbeck IV PK via subcutaneous delivery



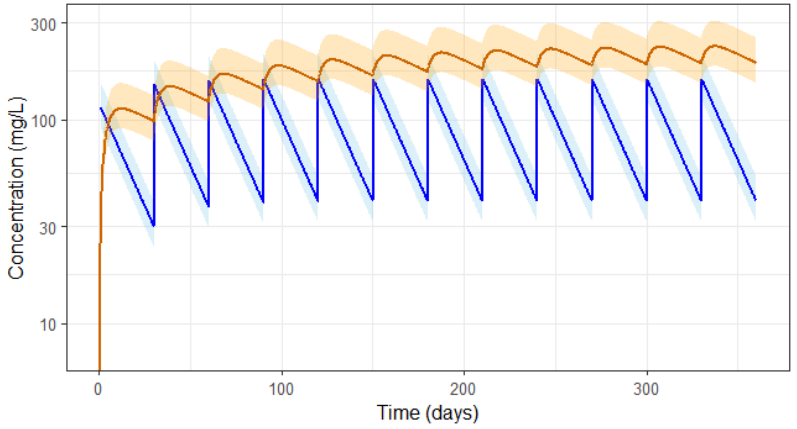
Demonstrated half-life extension in NHP pharmacokinetic (PK) studies with a mean half-life ranging from 21-27 days across doses and a modeled predicted human half-life of 70-80 days

Demonstrated >80% subcutaneous bioavailability in NHP

Bocunebart 750 mg IV (P2a high-dose) vs. SLTE-1009 QM SC



Bocunebart 480 mg IV (P2b high-dose) vs. SLTE-1009 QM SC

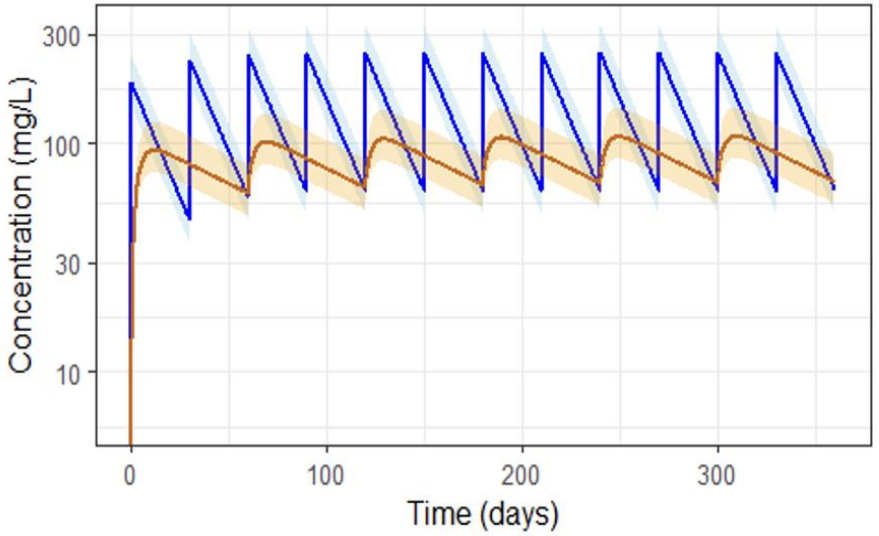


Modeling of expected human PK vs. bocunebart 750 (P2a) and 480 mg IV (P2b) shows possibility to match or exceed both C_{trough} and $C_{average}$ at 1-2 mL subcutaneous doses

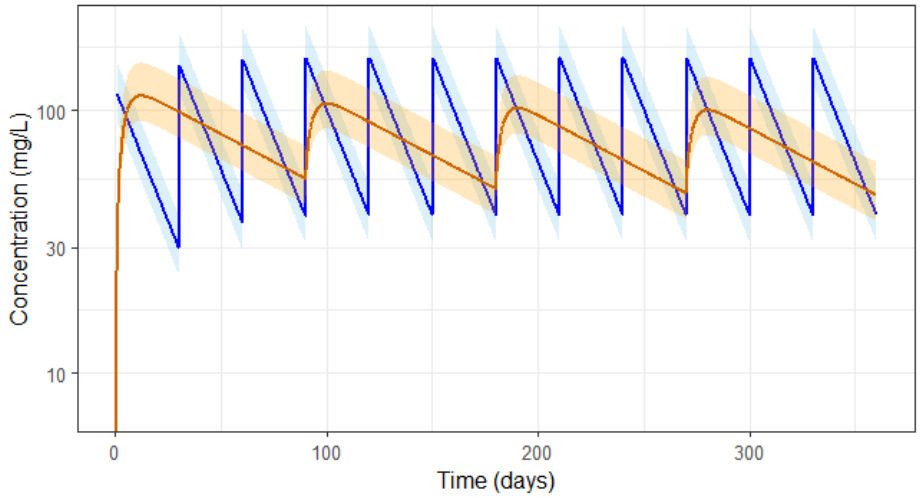
SLATE MEDICINES

SLTE-1009 has the potential for up to quarterly subcutaneous administration

Bocunebart 750 mg IV (P2a high-dose) vs. SLTE-1009 Q2M SC



Bocunebart 480 mg IV (P2b high-dose) vs. SLTE-1009 Q3M SC



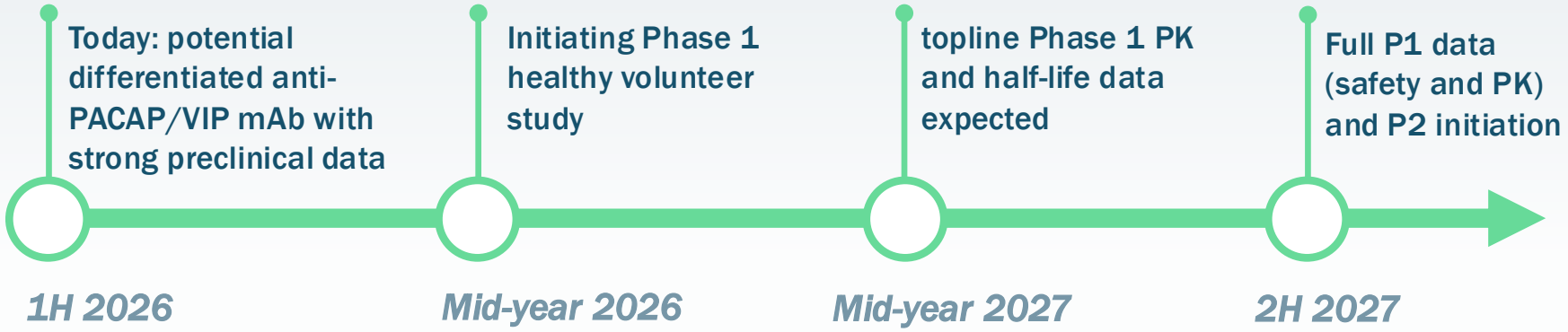
SLTE-1009 is modeled to potentially achieve Q3M dosing matching the high dose exposure from the Lundbeck P2b PROCEED trial and Q2M dosing matching the high dose from the Lundbeck P2a HOPE trial

Dose level and frequency expected to be evaluated in a Phase 2 dose-range finding study based on actual observed human pharmacokinetics in the Phase 1 healthy volunteer study

Q2M = Every 2 months dosing
Q3M – Every 3 months dosing

Slate has a potential path to early value creation and program derisking with Phase 1 PK

Potential Catalysts



Healthy volunteer PK has the potential to derisk subcutaneous administration demonstrating half-life extension

Additional pipeline program details on SLTE-2100 and undisclosed program expected to be announced in 2027

SLATE MEDICINES

Building a world-class migraine-focused biotech with a pipeline of potentially best-in-class, differentiated assets

- **SLTE-2100** An anti-PACAP/VIP x CGRP bispecific antibody
  - Complete blockade of three neuropeptides implicated in migraine, PACAP, VIP, and CGRP for potential differentiated efficacy in migraine prevention
  - Currently in lead optimization with DC nomination targeted for 2H26 and initiation of Phase 1 targeted for 2H27
- Undisclosed program is also intended for the treatment of migraine and other headache disorders with DC nomination targeted for 1Q28

Slate Medicines continues to evaluate additional assets focused on the prevention and treatment of migraine and other headache disorders in an effort to build a robust pipeline of differentiated assets

SLATE MEDICINES

Slate Medicines is a biotech company focused on expanding treatment options for migraine patients

Building a **world-class migraine-focused** biotech company

Lead asset SLTE-1009 is a potential **best-in-class subcutaneous anti-PACAP/VIP monoclonal antibody** for the prevention of migraine

Building a **pipeline of potentially differentiated assets** to broaden the treatment paradigm for migraine patients

Experienced team with a personal commitment to migraine

Backed by **top-tier life sciences investors**

SLATE MEDICINES