bridgebio

hope through
rigorous science

Autosomal Dominant Hypocalcemia Type 1 (ADH1) Investor Webinar

September 10, 2025

Encaleret is an investigational drug. Its safety and efficacy have not been fully evaluated by any regulatory authority.

Alexis and Jackson
Living with ADH1

Forward-Looking Statements and Disclaimer

Statements in this Presentation that are not statements of historical fact are considered forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Such forward-looking statements include, without limitation, statements regarding BridgeBio Pharma, Inc.'s (the "Company's") research and clinical development plans, commercialization and general strategy, regulatory matters, market size and opportunity, future financial position, future revenue, projected costs, prospects, plans, objectives of management, and the Company's ability to complete certain milestones. Words such as "believe," "anticipate," "plan," "expect," "intend," "will," "may," "goal," "potential," "should," "could," "aim," "estimate," "predict," "continue" and similar expressions or the negative of these terms or other comparable terminology are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. These forward-looking statements are neither forecasts, promises nor guarantees, and are based on the beliefs of the Company's management as well as assumptions made by and information currently available to the Company. Such statements reflect the current views of the Company with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company, including, without limitation, risks inherent in developing therapeutic products, the success, cost, and timing of the Company's product candidate research and development activities and ongoing and planned preclinical studies and clinical trials, the Company's value creation potential for patients, the potential market sizes and opportunities for encaleret, the safety, efficacy and mechanisms of encaleret, the potential of encaleret to treat ADH1 or HP, the success and timing of preclinical study and clinical trial results, the success of its clinical trial designs, the fact that successful preliminary preclinical study or clinical trial results may not result in future clinical trial successes and/or product approvals, , the Company's ability to obtain and maintain regulatory approval for its product candidates including encaleret, the Company's ability to obtain and maintain intellectual property protection for its product candidates including encaleret, the Company's financial position, the potency and safety of encaleret, the timing and expectations regarding results of the Company's various clinical trials, and those risks and uncertainties described under the heading "Risk Factors" in the Company's most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission ("SEC"), and "Risk Factors" in Item 1A of Part II of the Company's Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2025, filed with the SEC on April 29, 2025, and in subsequent filings made by the Company with the SEC, which are available on the SEC's website at www.sec.gov. In light of these risks and uncertainties, many of which are beyond the Company's control, the events or circumstances referred to in the forward-looking statements, express or implied, may not occur. The actual results may vary from the anticipated results and the variations may be material. You are cautioned not to place undue reliance on these forward-looking statements, which speak to the Company's current beliefs and expectations only as of the date this Presentation is given. Except as required by law, the Company disclaims any intention or responsibility for updating or revising any forward-looking statements made or contained in this Presentation in the event of new information, future developments or otherwise. No representation is made as to the safety or effectiveness of the product candidates for the therapeutic use for which such product candidates are being studied.

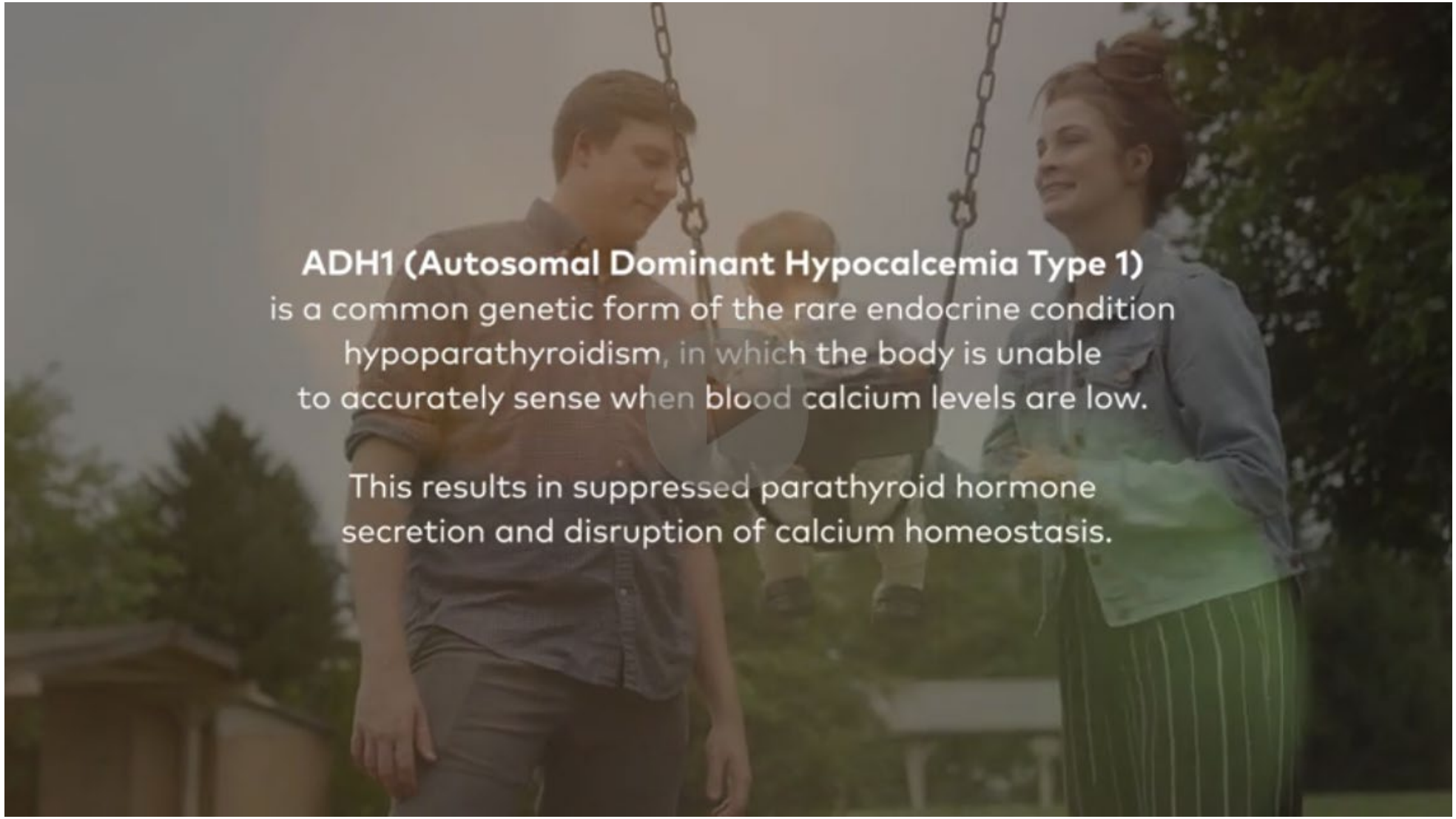
Certain information communicated in this Presentation may relate to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this Presentation, it has not independently verified, and makes 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 and certain other information 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. Finally, while the Company believes its own internal research is reliable, such research has not been verified by any independent source. The Company expressly disclaims any and all liability for any loss or damage (whether foreseeable or not) suffered or incurred by any person or entity as a result of anything contained in or omitted from this Presentation.

The Company is the owner of various trademarks, trade names and service marks. Certain other trademarks, trade names and service marks appearing in this Presentation are the property of third parties. Solely for convenience, the trademarks and trade names in this Presentation are referred to without the ® and TM symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Agenda

1	**Introduction**	Ananth Sridhar Chief Operating Officer BridgeBio Cardiorenal
2	**Overview of ADH1 & Encaleret**	Rachel Gafni, M.D. National Institute of Dental and Craniofacial Research of the National Institutes of Health (NIH)
3	**Review of Encaleret Clinical Development Program**	Scott Adler, M.D. Chief Medical Officer Calcilytix Therapeutics, a BridgeBio Company
4	**ADH1 Market Opportunity**	Ananth Sridhar Chief Operating Officer BridgeBio Cardiorenal
5	**Q&A Session**	

Patient Video - Jessica's Story



Overview of ADH1 & Encaleret

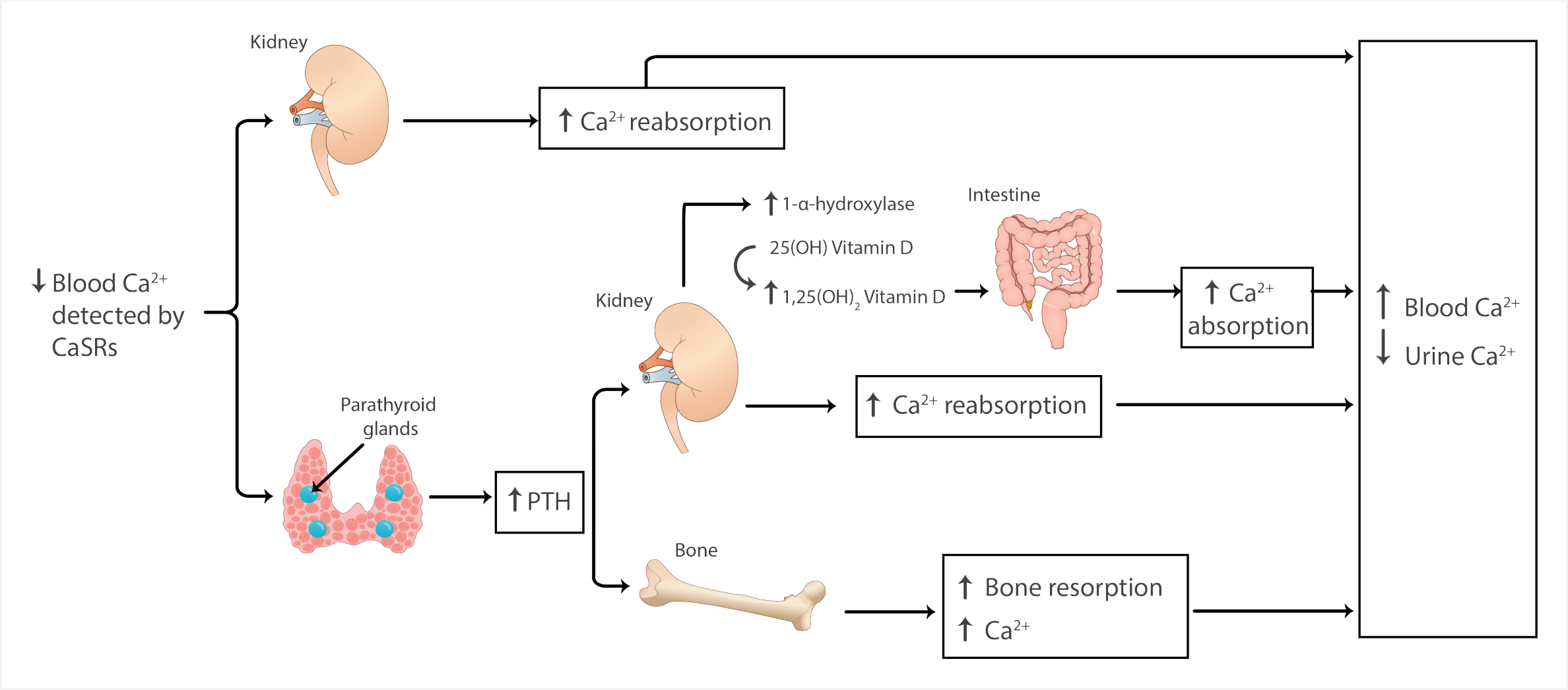
Rachel Gafni, M.D.

Senior Research Physician & CALIBRATE Study Steering Committee Co-Chair

National Institute of Dental and Craniofacial Research of the National Institutes of Health (NIH)

Encaleret is an investigational drug. Its safety and efficacy have not been fully evaluated by any regulatory authority.

Blood calcium is maintained by four organs regulated by the CaSR and parathyroid hormone

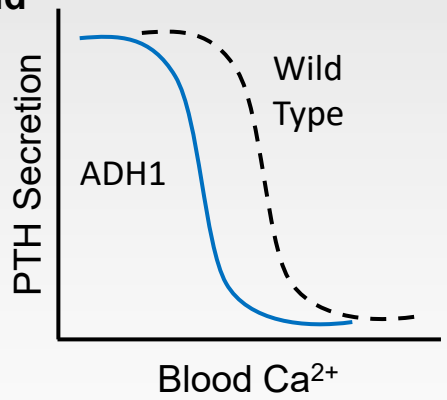


Ca^{2+} = ionized calcium; PTH = parathyroid hormone; CaSR = calcium-sensing receptor
Source: Roszko KL et al., J Bone Miner Res 2022.

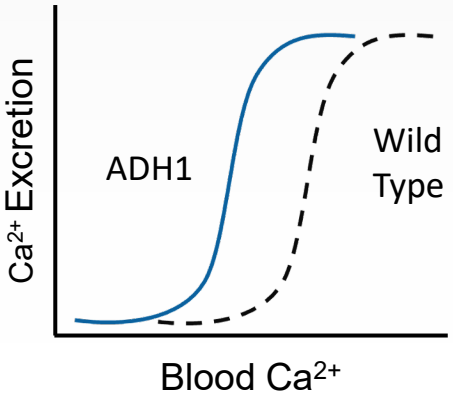
Activating variants in the *CASR* cause ADH1

Activating variants in the *CASR* increase tissue sensitivity to Ca^{2+}

Parathyroid



Kidney



Hyperactive CaSR causes dysregulation of Ca homeostasis

- PTH ↓ — **Decreased parathyroid hormone (PTH) secretion**
- Ca^{2+} ↓ — **Decreased blood calcium**
- Ca^{2+} ↑ — **Increased urinary calcium**

Clinical Manifestations

Acute symptoms

Hypocalcemic seizures

Paresthesia

Tetany

Muscle cramps

Long-term complications

Nephrolithiasis

Nephrocalcinosis

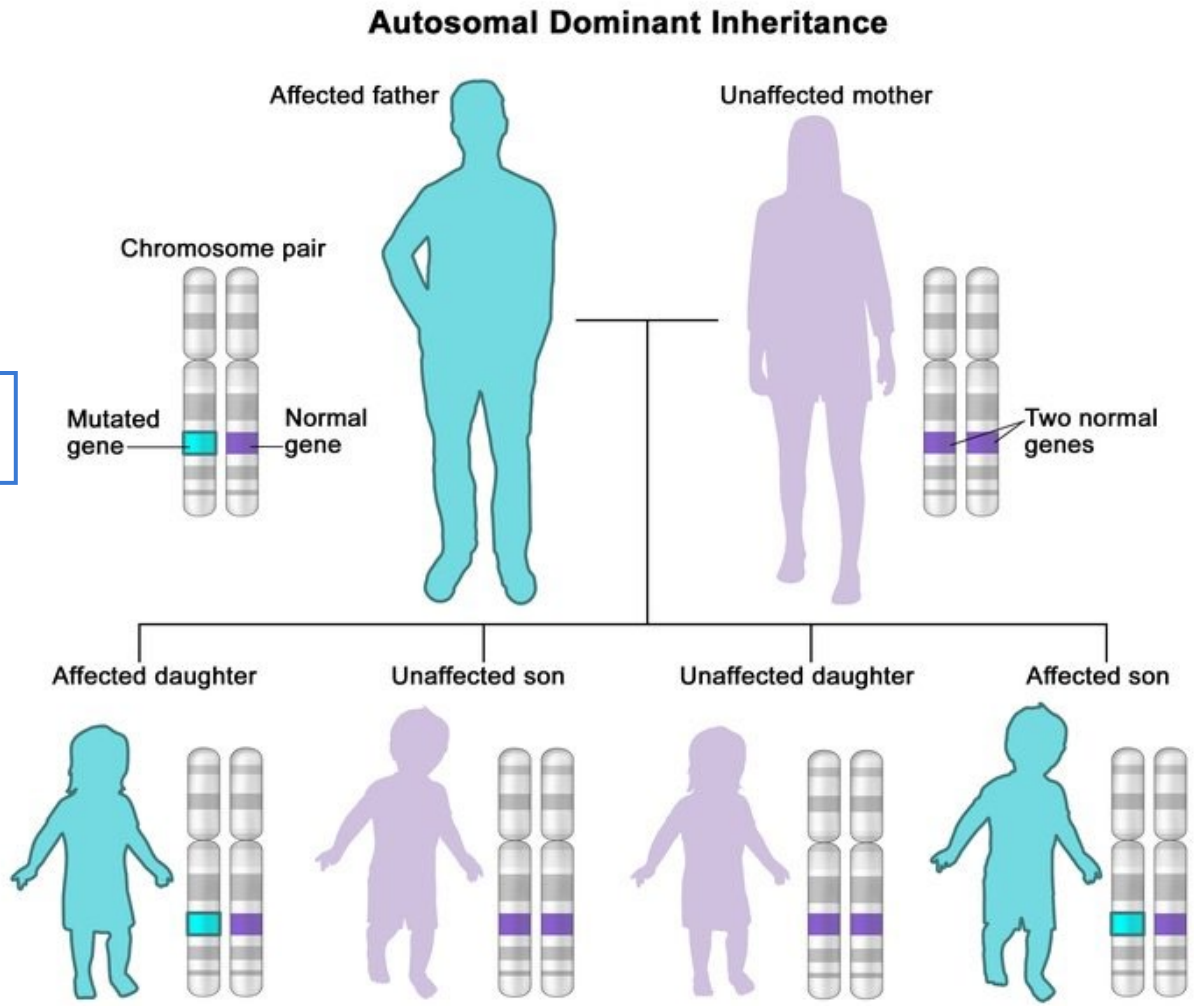
Chronic Kidney Disease

Conventional therapy with calcium and activated vitamin D does not correct the underlying pathophysiology and has the potential to worsen long-term complications

Source: Roszko KL et al., J Bone Miner Res 2022.

CASR variants associated with ADH1 are commonly inherited in an autosomal dominant pattern

Change in ***CASR*** gene



- A single altered copy of the gene is enough to cause the condition
- Each child has a 50% chance of inheriting the condition
- It is common for someone with ADH1 to be the first person in a family to be diagnosed; the variants can be passed on to future generations

Source: *NCI Genetics Dictionary*

Diagnosis of ADH1

Definitive diagnosis of ADH1 requires genetic testing[1]

Medical History (Patient and Family)[1,2]

+

Clinical Features[2,3]

+

Genetic Testing[2,3]

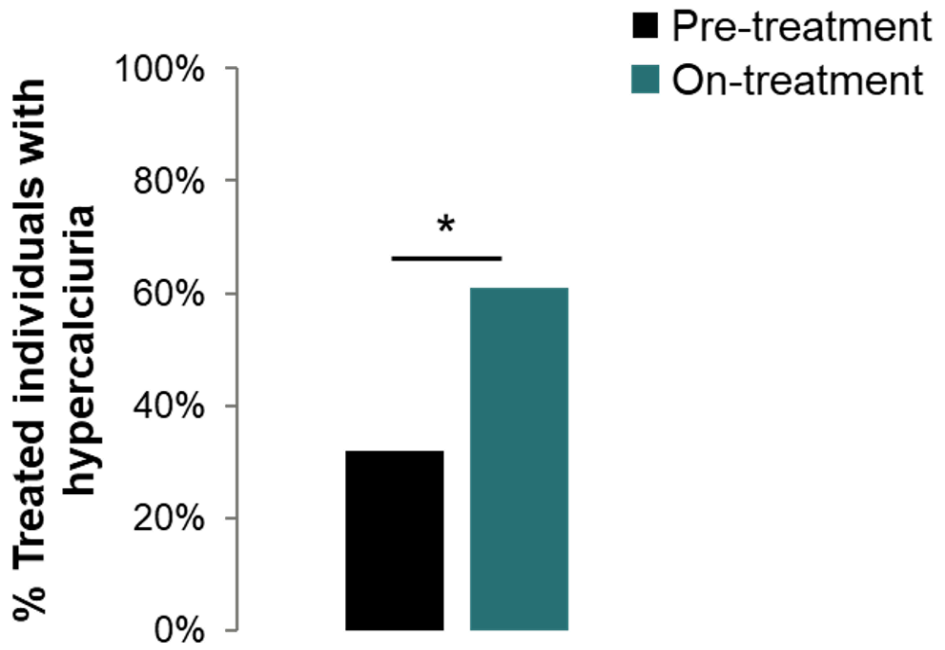
- ADH1 prevalence is estimated to be 1 in 25K based on general population genetics evidence[4,5]
- ADH1 can be difficult to diagnose based on symptoms alone and patients often face a prolonged delay before receiving a final diagnosis
- Family screening is recommended in an ADH1 diagnosis due to its dominant inherence pattern[1,4]
- According to a systematic literature review, the median age of a diagnosis of a hypocalcemia-related disorder is 4, but a genetically confirmed diagnosis of ADH1 is delayed with a median age of 25 years[6]

1. Bilezikian et al., J Bone Miner Res 2011. 2. Khan et al., J Bone Miner Res 2022. 3. Mannstadt et al., J Bone Miner Res 2022. 4. Dershem, et al. Amer Jour of Hum Genetics, 2020. 5. Chang, et al. Am J Hum Genet., 2025. 6. Roszko et al., J Bone Miner Res 2022.

Management of patients with ADH1 – Conventional therapy

- Includes calcium supplements and activated vitamin D
  - Calcium 3-4x/day
  - Active vitamin D 1-2x/day
- Some patients also require magnesium and potassium supplements
- ↑ blood calcium = ↑ urine calcium
- Goal to maintain blood calcium as low as tolerated to
  1. Alleviate symptoms of hypocalcemia
  2. Minimize hypercalciuria
- Patients often continue to experience hypocalcemia-related symptoms

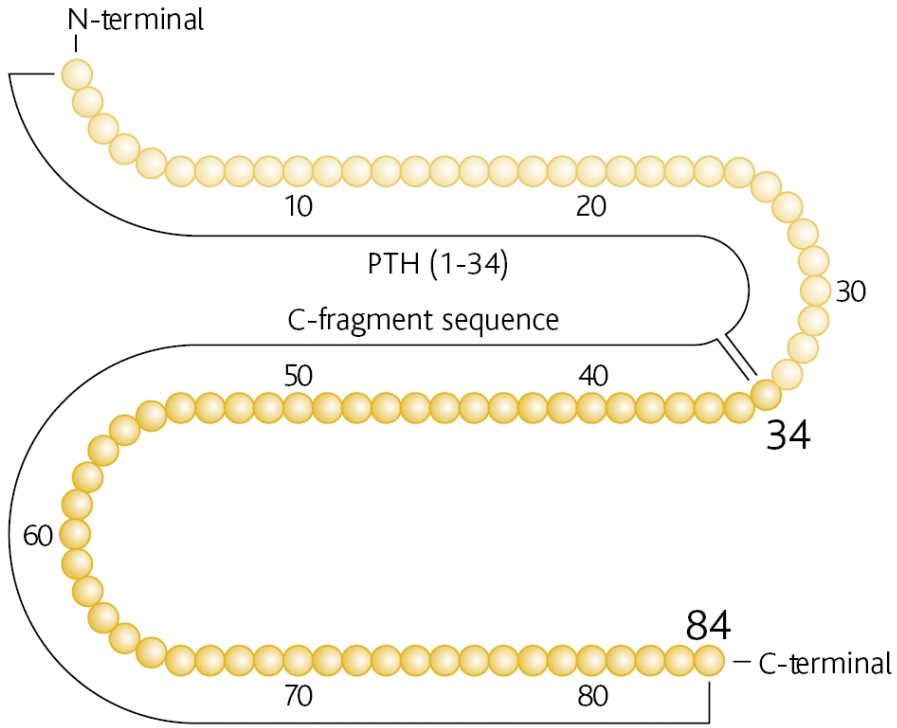
Effects of conventional therapy on calcium excretion



*p = 0.0433. Statistical significance was determined using a McNemar's test.

Source: Roszko KL et al., J Bone Miner Res 2022.

Why is PTH replacement inadequate for ADH1?



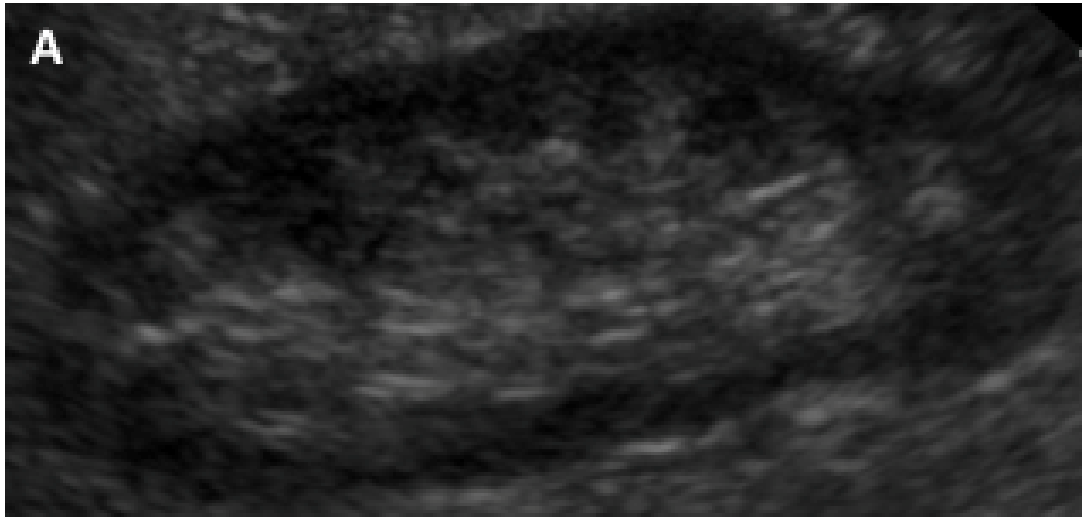
Schematic image showing the 84 amino acids of human parathyroid hormone
Image Source: Public domain

- Most studies of PTH analogs have deliberately excluded ADH1 patients
- ADH1 patients have capacity to secrete endogenous parathyroid hormone; PTH analogs may suppress this response
- Cases of long-acting PTH analog use in ADH1 patients did not sufficiently restore mineral homeostasis[1,2]

1. Chondrogianni, M.E., ESPE ESE Scientific Sessions, 2025. 2. Zygmunt, A., ENDO Scientific Sessions, 2025.

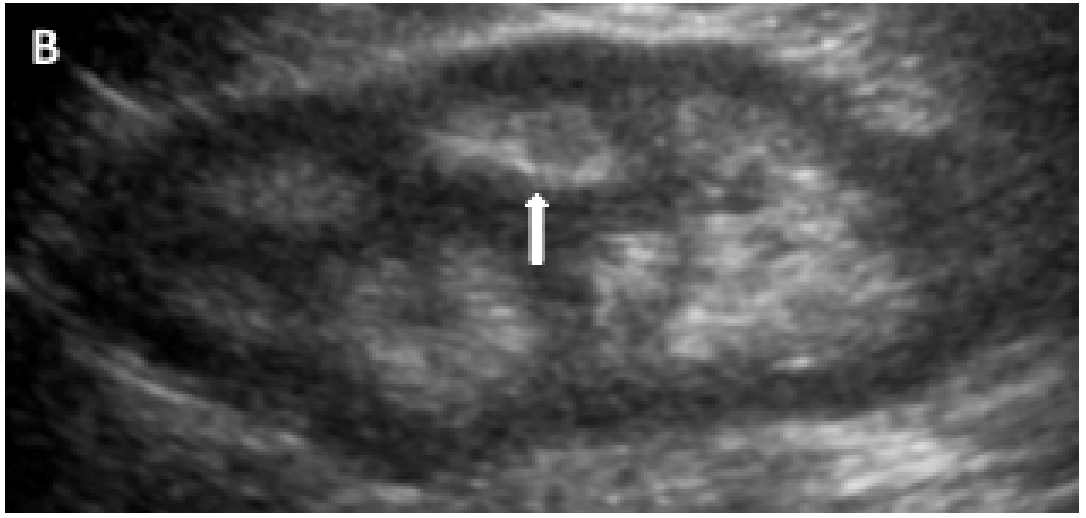
Twice daily PTH 1-34 did not prevent nephrocalcinosis in this ADH1 patient

Baseline



Normal kidney ultrasound

One year of PTH 1-34 BID



Medullary nephrocalcinosis

- Open label study of BID PTH 1-34
- N=31, 4 participants with ADH1
- Blood calcium levels maintained low/low normal (7.6-9 mg/dL/1.9-2.25 mmol/L)

Source: Gafni et al., J Bone Miner Res 2018

Encaleret, an investigational oral calcilytic, may be a potential treatment for ADH1

- Encaleret is an investigational negative allosteric modulator of the CaSR that can decrease CaSR sensitivity to extracellular calcium
- Normalizing CaSR sensitivity could correct hypocalcemia, hypercalciuria, and low PTH in individuals with ADH1

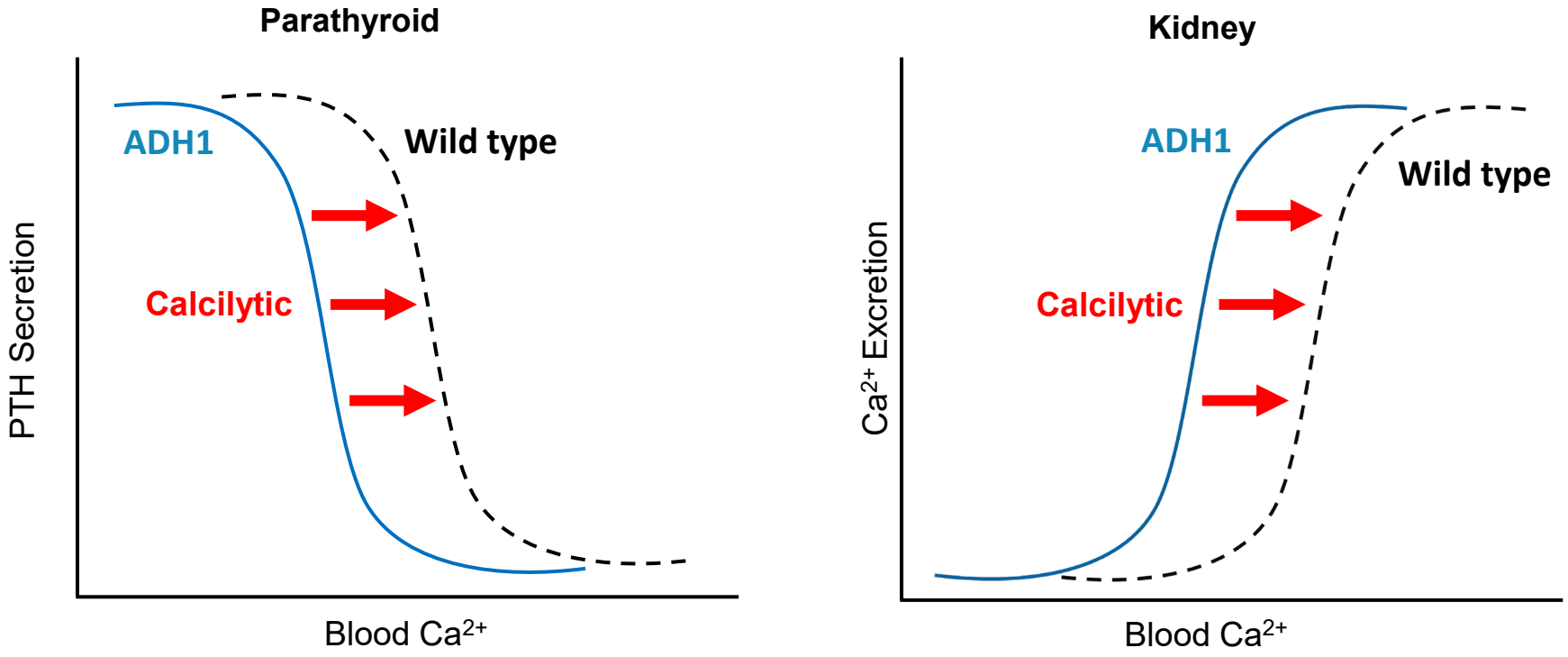


Figure adapted from Tfelt-Hansen J, et al. Curr Med Chem. 2002.
Encaleret is an investigational drug. Its safety and efficacy have not been fully evaluated by any regulatory authority.

Encaleret Clinical Development Program

Scott Adler, M.D.

Chief Medical Officer

Calcilytix Therapeutics, a BridgeBio Company

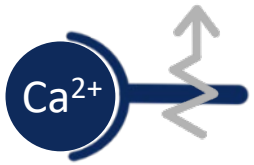
Encaleret is an investigational drug. Its safety and efficacy have not been fully evaluated by any regulatory authority.

Encaleret is a first-in-class, disease-modifying investigational therapy that targets the underlying disease mechanism of ADH1

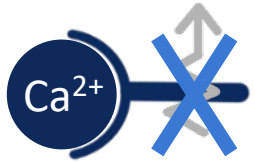
Mechanism

Normal CaSR senses and regulates serum Ca levels to maintain homeostasis

Encaleret is a **CaSR antagonist** designed to decrease the sensitivity of CaSRs to extracellular calcium



ADH1 CaSR is overly sensitive to extracellular calcium



CaSR sensitivity restored in the presence of encaleret

Overactive CaSR causes dysregulation of calcium homeostasis, **encaleret** has the potential to normalize PTH, serum Ca, and urine Ca levels

Restore *PTH to the normal range*

Restore *serum calcium to the normal range*

Decrease *urine calcium to the normal range*

Design Principles

First and only investigational treatment directly targeting ADH1 at its source

Potential to restore physiologic mineral homeostasis that is disrupted by CaSR oversensitivity

Address common symptomology

Designed to normalize PTH, serum Ca, and urine Ca levels, potentially resolving key symptoms

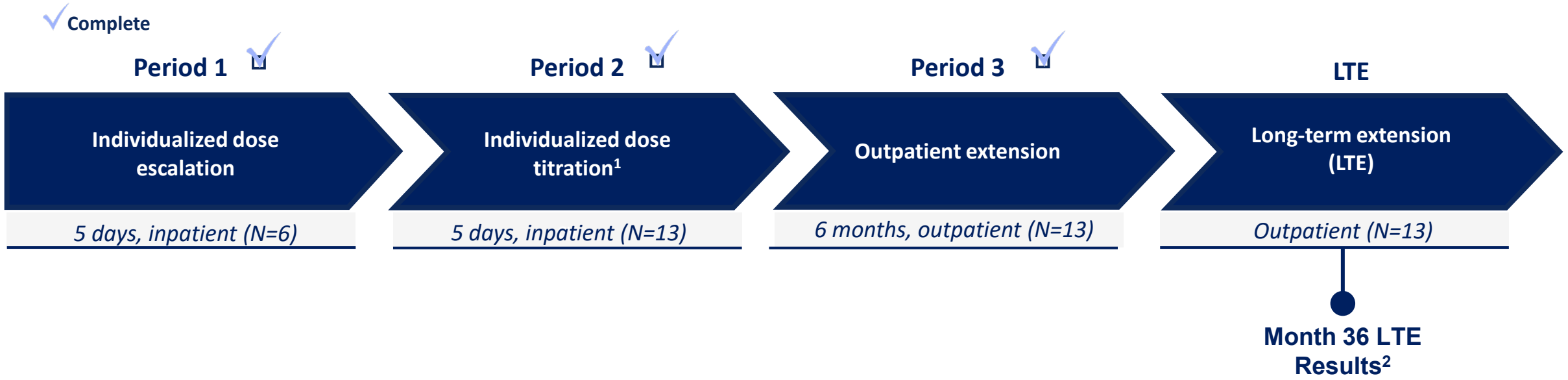
Convenient oral dosing

First targeted treatment for ADH1 in a convenient form for patients and providers

CaSR = Calcium Sensing Receptor; Ca = Calcium; PTH = Parathyroid Hormone.

Phase 2 study evaluated encaleret in 13 ADH1 patients

Program Overview



Key study objectives:

- Safety and tolerability
- Blood calcium concentration
- Urine calcium concentration
- Intact parathyroid hormone concentration

Additional measures:

- Blood 1,25-$(OH)_2$-vitamin D, magnesium, and phosphate
- Urine creatinine, cAMP, citrate, phosphate, sodium, magnesium
- Bone turnover markers (serum collagen C-telopeptide, serum procollagen Type 1 N-propeptide)

[1]Encaleret doses titrated to blood calcium and phosphorus levels. [2]Month 36 LTE (N=13) results presented at ENDO 2025.
Standard of care (calcium and active vitamin D) was discontinued prior to the first encaleret dose

Baseline Characteristics

Characteristic	Study Population (N = 13)	*Normal Range*
Age, mean, yr (range)	39 (22-60)	
Female, n (%)	8 (62%)	
Corrected Calcium[1,2] (mg/dL)	7.1 ± 0.4	8.4 –10.2
Intact PTH (pg/mL)	6.3 ± 7.8	15 – 65
Phosphate (mg/dL)	4.5 ± 1.1	2.3 – 4.7
Magnesium (mg/dL)	1.7 ± 0.2	1.6 – 2.6
24h Urine Calcium (mg/24h)	384 ± 221	< 250 - 300
Nephrocalcinosis/Nephrolithiasis, n (%)	10 (77%)	
eGFR (mL/min/1.73 m^2)	84 ± 25	>60
Supplements		
Elemental Calcium (mg/day) [mean (range)]	2120 (750-4800)	
Calcitriol (µg/day) [mean (range)]	0.7 (0.2-2.0)	
***CASR* Variants**	**C131Y (2), P221L (2), E604K (1), A840V (3), F788C (1), T151M (1), Q245R (1), I692F (1), E228K (1)**	

Gafni RI et al., NEJM 2023
Data reported as mean±SD. eGFR = estimated glomerular filtration rate calculated by the CKD-EPI equation.

1. Albumin-corrected calcium. 2. Measurements taken pre-dose Day 1, Period 2.

Encaleret was generally well-tolerated over 42 months of outpatient administration

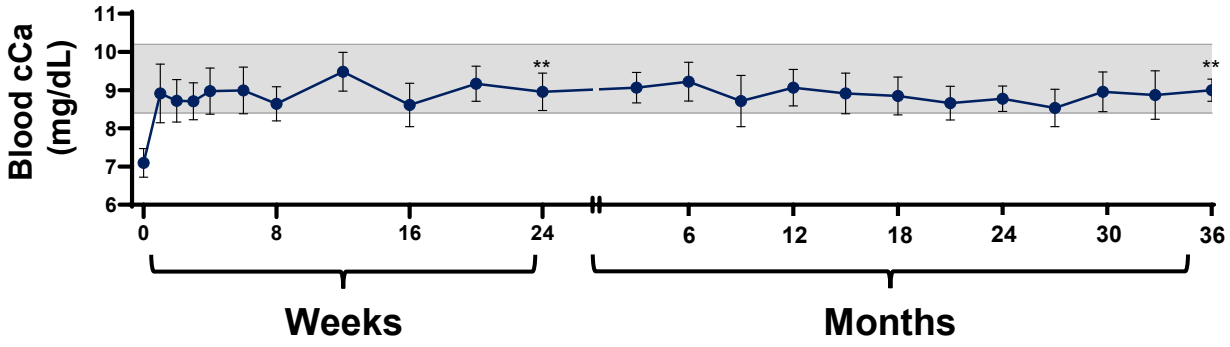
	Periods 2 and 3 N=13	LTE N=13
Number of subjects experiencing any Serious Adverse Event	**0 (0%)**	**2 (15%)**
Post-operative right shoulder pain		1
Chest pain		1
Number of subjects experiencing any Treatment-Emergent Adverse Event (TEAE)	**13 (100%)**	**13 (100%)**
Mild	13 (100%)	13 (100%)
Moderate	2 (15%)	8 (62%)
Severe	0	1 (8%)
Number of TEAEs Reported	**81**	**153**
Mild	79 (98%)	121 (79%)
Moderate	2 (2%)	31 (20%)
Severe	0	1 (1%)
Treatment-related TEAEs[1]	**16 (20%)**	**2 (1%)**
Hypophosphatemia	10 (63%)	0
Hypercalcemia	6 (37%)	2 (100%)

Source: Gafni R., et al., NEJM, 2023; 389:1245-1247. Gafni R., et al., Jour Endo Soc., 2023; 7(Suppl 1).
Data as of Mar 3, 2025. [1]Treatment-related TEAEs were transient and resolved either spontaneously or with adjustment of the encaleret dose. Treatment-related TEAEs were counted as the number of events per period and are presented as a percentage of the total number of TEAEs.

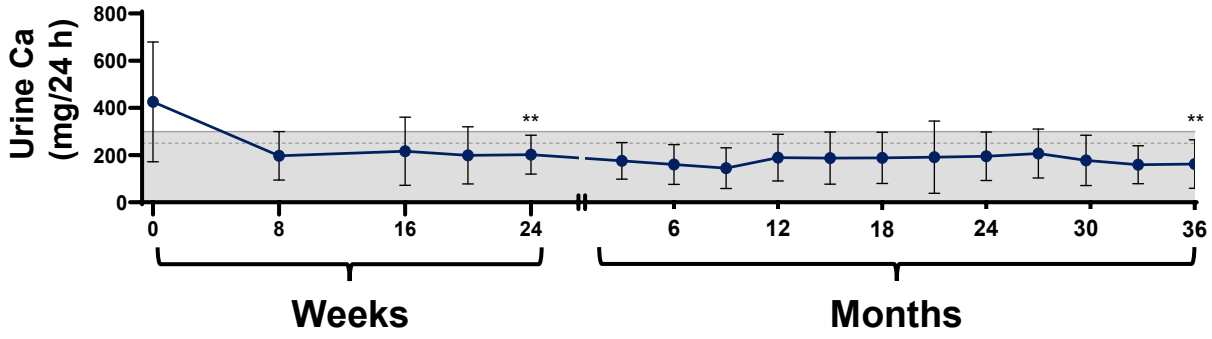
Phase 2 results showed rapid and sustained normalization of serum Ca, urine Ca, and PTH

Normal Range

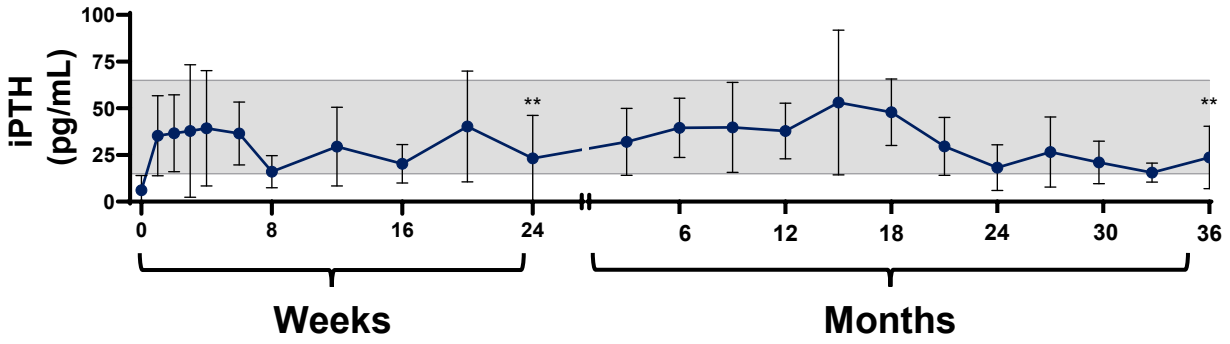
Blood Calcium



Urine Calcium



PTH



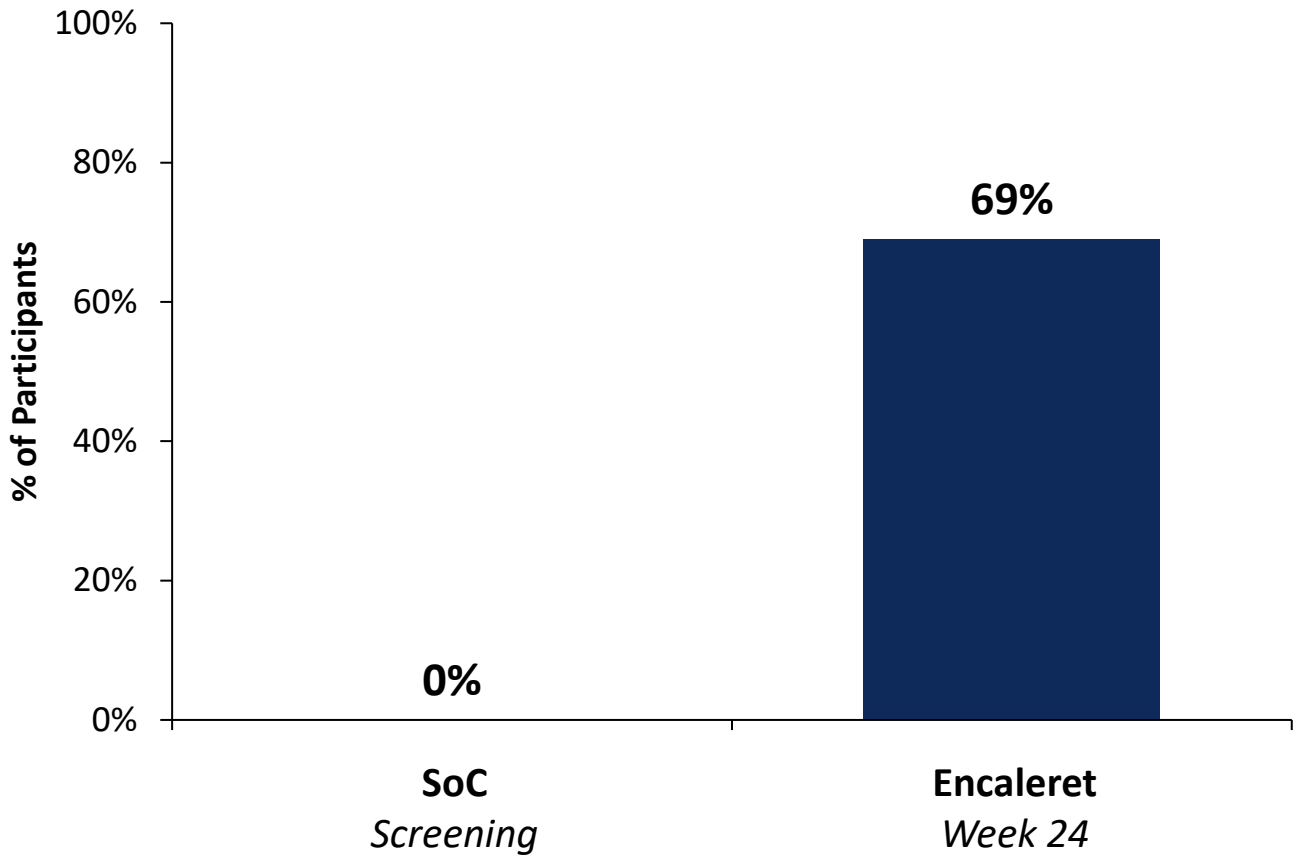
Encaleret corrected mean blood calcium, PTH, and urine calcium in participants with ADH1 over a 42-month period

Source: Gafni R., et al., NEJM, 2023; 389:1245-1247. Gafni R., et al., Jour Endo Soc., 2023; 7(Suppl 1).
Data reported as mean+SD. Values below limit of assay quantitation recorded as "0". Gray shading reflects normal range. Solid line for urine calcium reflects the upper limit for men and dashed line reflects upper limit for women. Values shown for weeks 0, 8, 16, and 24 are pre-encaleret. ** p-value < 0.01 Week 24 and LTE Month 36 compared to Baseline.

69% of participants responded to encaleret as defined by the planned Phase 3 primary analysis

Individuals achieving both blood Ca and urine Ca in the target range

SoC vs Encaleret (n=13)



Ca = calcium; SoC = standard of care (calcium and active vitamin D)

Summary of encaleret Phase 2 results and ongoing development

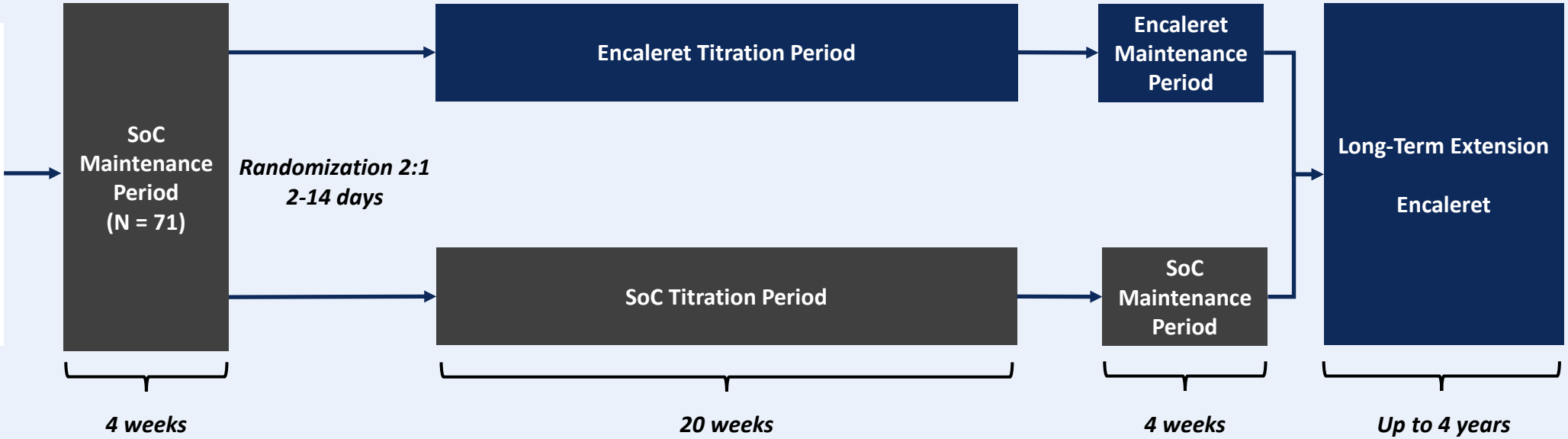
- Existing treatment regimens for patients with ADH1 focus on symptom management rather than addressing the underlying disease mechanism
- Patients with ADH1 face significant unmet needs that may be addressed by precision therapies targeting the underlying CaSR-driven pathophysiology
- In patients with ADH1, encaleret administered twice daily rapidly corrected and maintained mineral homeostasis within the normal range, as assessed by:
  - ✓ Increase in endogenous intact PTH
  - ✓ Correction of hypocalcemia
  - ✓ Normalization of mean 24-hr urine calcium
  - ✓ Reduction in mean blood phosphate
  - ✓ Increase in mean blood magnesium
- Encaleret was well-tolerated over 42 months of outpatient administration
- Results support ongoing evaluation of encaleret in ADH1 patients in the Phase 3 CALIBRATE study

Topline results of the CALIBRATE Phase 3 study of encaleret in ADH1 are anticipated in Fall 2025

CALIBRATE

Screening and SoC Optimization Period

- Age ≥ 16 years of age
- Documented pathogenic or likely pathogenic activating variant, or variant of uncertain significance, of the *CASR* gene associated with biochemical findings related to hypoparathyroidism



Primary Endpoint:

- Proportion of participants achieving:
  - Blood Ca within the target range **AND**
  - 24-hour urine Ca within the reference range

Select Secondary Endpoints:

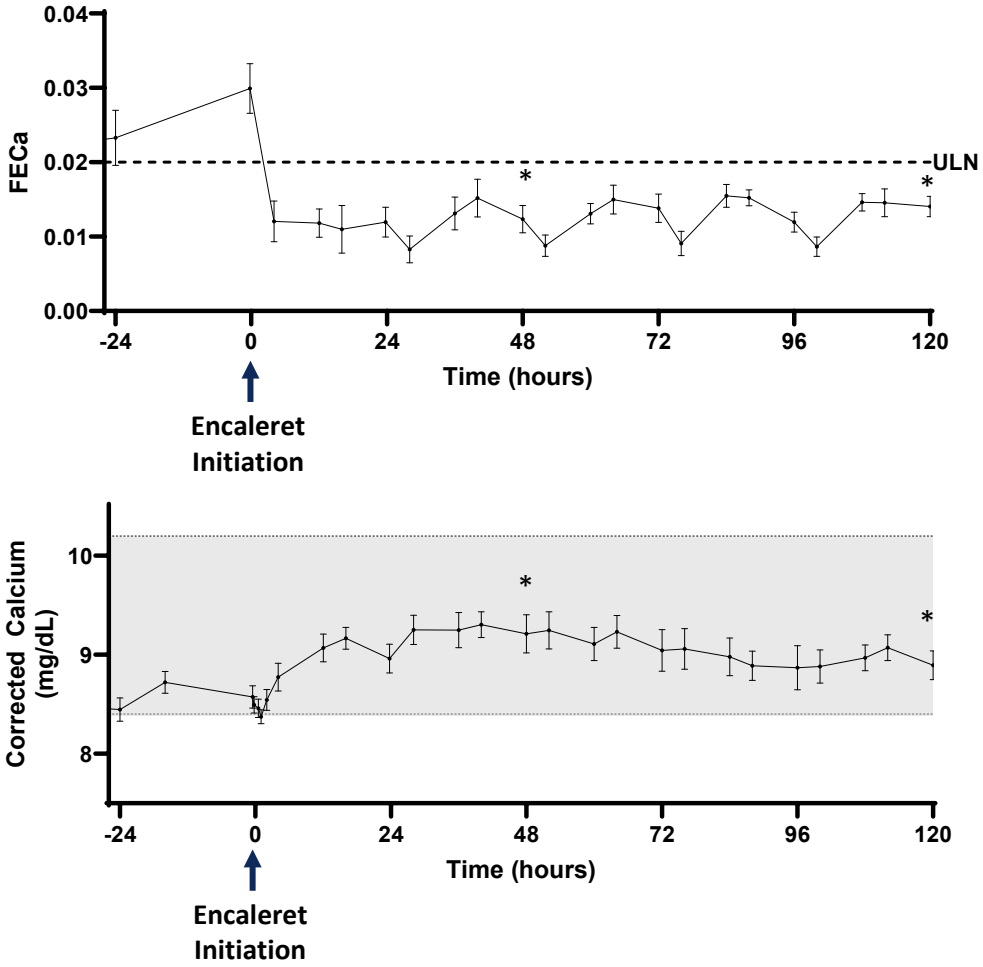
- Blood iPTH, 1,25-$(OH)_2$ Vitamin D, magnesium, and phosphate
- Urine magnesium and phosphate
- Bone turnover markers
- Renal ultrasound and renal function
- ER/urgent care visits and/or hospitalizations
- Quality of life (SF-36)

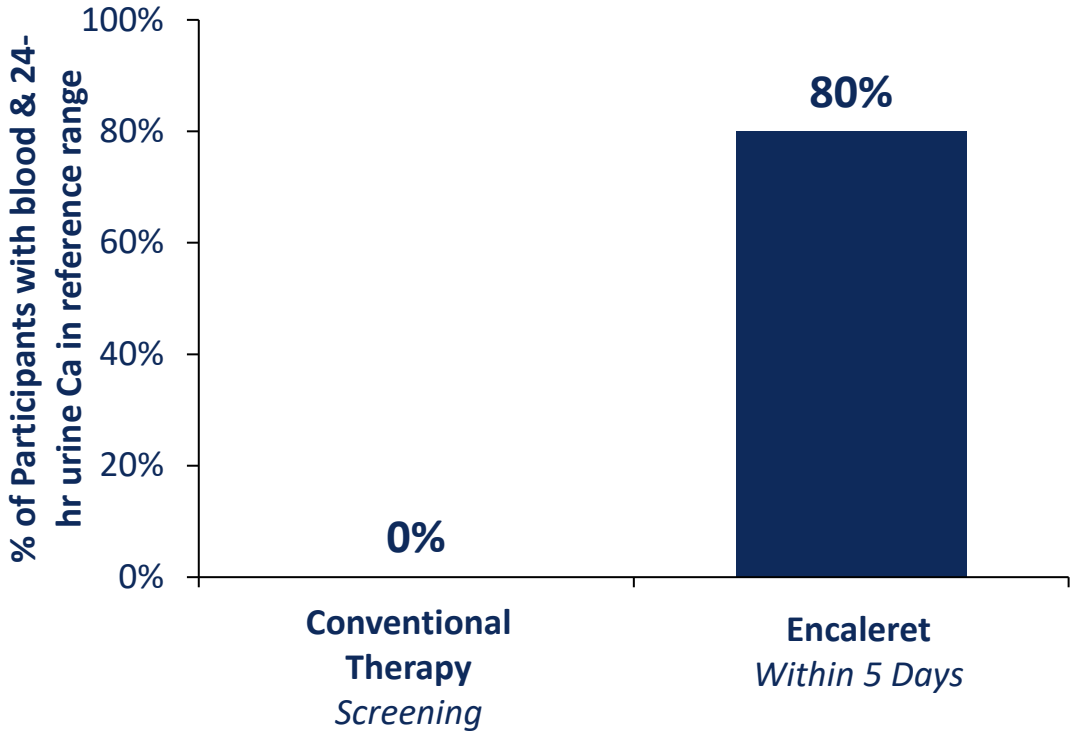
LPLV has occurred; CALIBRATE Study Topline Results Expected in Fall 2025

SoC = standard of care; a combination of oral activated Vitamin D and/or calcium supplements. *CASR* = calcium-sensing receptor gene.

Preliminary data demonstrate rapid, PTH-independent, effect on blood and urine calcium

Proof-of-principle phase 2 study of encaleret in post-surgical hypoparathyroidism (PSH), N=10





*p<0.05, 48hr or 120hr compared to baseline at 0hr .
FECa= fractional excretion of calcium, a measure of renal calcium handling; ULN = upper limit of normal. Gray shading reflects normal range.
Source: Hartley I.R. et al., presented at ASBMR 2025 Annual Meeting.

Proof-of-concept study findings are suggestive of a potential path for improved calcium control in a convenient pill form

Potential Differentiating Features For Encaleret

- Orally administered tablet
- Benefit in 24-hour urinary calcium excretion
- Avoidance of long-term PTH-mediated impact on bone health

ADH1 Market Opportunity

Ananth Sridhar

Chief Operating Officer,
BridgeBio Cardiorenal

There are no therapies specifically indicated for ADH1, a serious and rare genetic condition

12K Individuals with ADH1
~12K ADH1 prevalent population in the US based on 4 population databases[1-2]

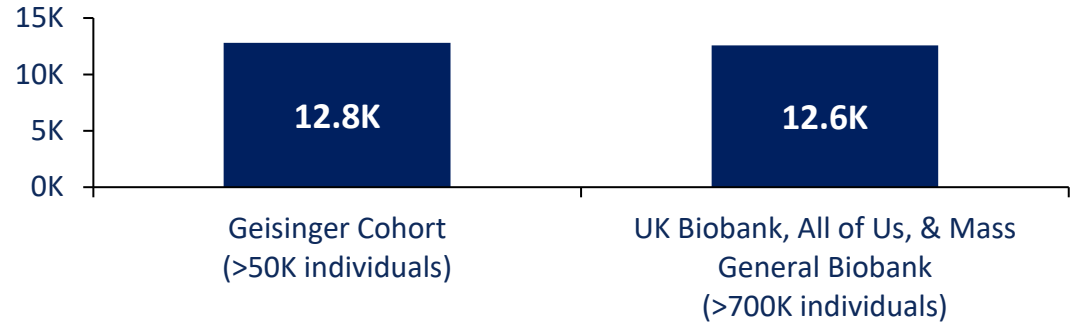
9K Symptomatic
73% of patients with ADH1 are symptomatic[3]

3K – 5K Currently Addressable
40-60% of symptomatic ADH1 patients are estimated to be diagnosed today, anticipate increase

An analogous ADH1 market is XLH

	XLH	ADH1
Prevalence (US)	12K[5]	12K
Disease burden	Hypophosphatemia	Acute - hypocalcemia Chronic - hypercalciuria
Standard of care	Vitamin D, daily phosphate	Vitamin D, daily calcium
Registrational endpoint	Serum phosphate	Blood and urine calcium
Projected peak year sales	$2B+[6]	$1B+

ADH1 variant frequency estimates in literature[1-2]



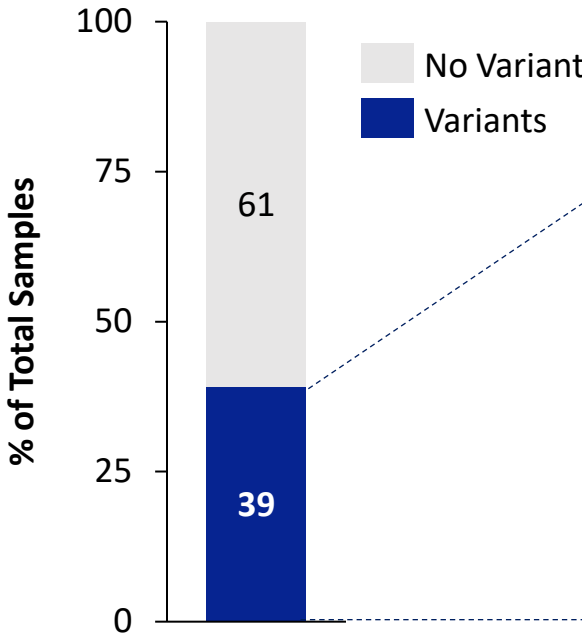
[1]Dershem, et al. Amer Jour of Hum Genetics, 2020. [2] Chang, et al. Am J Hum Genet., 2025. [3]Roszko, et al. JBMR. 2022. [5]Dahir, et al. Jour Endo Soc., 2020. [6]Evaluate Pharma. XLH = x-linked hypophosphatemia.

ADH1 is emerging as the leading isolated cause of nonsurgical hypoparathyroidism[1]

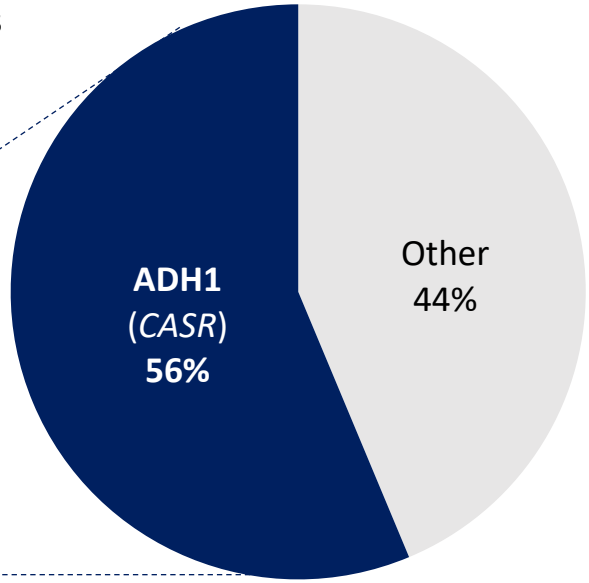
Results – Sponsored Genetic Testing Program

Characteristics	Sample Population (N=169)
Mean Age (range)	23.4 (0-81)
Program Entry Criteria	
Diagnosis of nonsurgical/idiopathic hypoparathyroidism	73.9%
Diagnosis of hypocalcemia suspected to be of a genetic cause	23.7%
Had a relative with a confirmed diagnosis of genetic hypoparathyroidism	2.4%

Variants in Nonsurgical HP Individuals



Relative Number of Individuals with Detected Variants[2]



ADH1 was found to be the most common cause of isolated nonsurgical hypoparathyroidism (~20% of all cases)

[1]Mannstadt et al., ENDO Annual Conference, 2023. [2]The hypoparathyroidism panel consists of 26 genes associated with the condition: ACADM, AIRE, ATP1A1, CASR, CHD7, CLDN16, CLDN19, CNNM2, DHCR7, EGF, FAM111A, FXYD2, GATA3, GCM2, GNA11, HADHA, HADHB, KCNA1, NEBL, PTH, SEMA3E, SLC12A3, SOX3, TBCE, TBX1, TRPM6.

Evolution in the diagnosis and management of hypoparathyroidism may further accelerate ADH1 market development

Sponsored Genetic Testing Program

Detect Hypopara

No-cost genetic testing available for providers & patients

Established ICD-10 Code dedicated to ADH1 & ADH2

E20.810

Billable ICD-10 code associated with ADH1 & ADH2

Management Guidelines Specify Need for Genetic Testing[1]

"Genetic testing is advised for all patients with idiopathic HypoPT, especially in the presence of a family history of HypoPT and in those under the age of 40 years"

Encaleret has a first-in-class market opportunity to re-establish the standard of care in ADH1 while benefiting from ecosystem tailwinds supporting patient identification

[1]Khan, A., et al., Metabolism, 2025; 171:156335.

The primary analysis of CALIBRATE will assess the relative improvement of blood and urine calcium on encaleret compared to SoC

Base Case Target

- Statistically significant primary analysis result compared to SoC
- Restoration of endogenous PTH secretion
- Comparable safety and tolerability profile to SoC

Upside Target

- Statistically significant primary analysis result compared to SoC
- At week 24, ≥50% of study participants achieve target blood and urine Ca on encaleret
- Majority of participants randomized to encaleret able to remain independent from SoC
- At week 24, mean PTH within normal range on encaleret
- Comparable safety and tolerability profile to SoC

Q&A Session