



NEWS RELEASE

Novel Human Genetics Evidence Confirms Estimates of Genetic Prevalence, Underdiagnosis, and Potentially Greater Symptom Burden of Gain-of-Function CASR Variants Associated with ADH1

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- By examining over 100 unique variants associated with the CASR gene causative of ADH1, the average frequency of gain-of-function CASR variants was ~3.7 per 100,000, closely aligned to previously published estimates¹ (3.9 per 100,000), which equates to approximately 25,000 carriers of ADH1-causing variants in the US and EU
- Only ~20% of individuals with genetic variants linked to ADH1 were found to have an established diagnosis, highlighting a major gap in disease recognition and care
- Nine novel gain-of-function CASR variants were identified, which were associated with a symptom burden consistent with the known clinical presentation of ADH1
- The findings show an allelic series, indicating that CASR regulates calcium homeostasis in ADH1 and more complex disorders of calcium metabolism, such as chronic hypoparathyroidism

PALO ALTO, Calif., July 23, 2025 (GLOBE NEWSWIRE) -- BridgeBio Pharma, Inc. (Nasdaq: BBIO) ("BridgeBio" or the "Company"), a new type of biopharmaceutical company focused on genetic diseases, published an analysis of genetic and health data from more than 700,000 individuals in the **American Journal of Human Genetics**, confirming prior estimates of the genetic prevalence of autosomal dominant hypocalcemia type 1 (ADH1) and underscoring opportunities to elevate diagnostic suspicion.

“ADH1 is a common genetic form of the rare endocrine disorder hypoparathyroidism. ADH1 is caused by activating variants in the calcium-sensing receptor gene (CASR) and presents as hypocalcemia that can cause serious symptoms like seizures, irregular heart rhythms, muscle cramps, and breathing problems. This study confirms estimates of the genetic prevalence of ADH1 across four biobanks and reveals that many affected individuals remain undiagnosed. The study illuminates a critical gap in recognizing and diagnosing ADH1 and providing appropriate care. Beyond expanding the number of genetic variants linked to ADH1, this work reinforces the vital role of genetic testing in uncovering the underlying cause of hypoparathyroidism,” said Dr. Michael Mannstadt of Massachusetts General Hospital and Harvard Medical School.

“ADH1 is a genetic condition that is often misdiagnosed or overlooked, taking a toll on an individual's quality of life due to mismanaged symptoms. These findings show that ADH1 is more prevalent and underdiagnosed than we thought and it is important to raise awareness around genetic testing to identify the root cause of a condition to help manage symptoms and improve quality of life. This is a step towards closing the gap in care by potentially providing a diagnosis earlier and more easily, addressing a constant concern of the community,” said Patty Keating, Executive Director of HypoPARAthyroidism Association, a non-profit patient association supporting and advocating for people impacted by hypoparathyroidism.

CALIBRATE, BridgeBio's Phase 3 clinical trial of encaleret for ADH1, a condition caused by activating variants of the CASR, is fully enrolled with 71 participants. The registrational study is the largest prospective interventional study ever to be conducted in ADH1. The Company expects to report topline results in the second half of 2025. If successful, encaleret would be the first approved therapy for individuals living with ADH1. The Company also intends to initiate a registrational study of encaleret in chronic hypoparathyroidism, another condition linked with the newly found CASR allelic series, in 2026.

About Autosomal Dominant Hypocalcemia Type 1 (ADH1)

ADH1 is caused by gain-of-function variants of the CASR gene encoding the CaSR. The calcium-sensing receptor regulates the extracellular calcium concentration in the body primarily through its activity in the parathyroid glands and the kidney. Due to increased sensitivity of the variant CaSR to extracellular calcium, patients with ADH1 have low blood calcium (hypocalcemia), inappropriately low parathyroid hormone levels, and excess excretion of calcium in the urine (hypercalciuria). Hypocalcemia can cause neuromuscular symptoms, which can include severe muscle cramping and seizures, while hypercalciuria can lead to kidney calcifications and impaired kidney function.

Studies estimate that there are 25,000 carriers of gain-of-function variants of the calcium-sensing receptor (CaSR) gene, the underlying cause of ADH1, in the U.S. and EU. This estimate is based on analyses of independent general population genetic datasets, including Geisinger Health System, UK Biobank, gnomAD, All of Us, TopMed, and Mass General Brigham Biobank.^{1,2}

About Encaleret

Encaleret is an investigational, orally administered small molecule under investigation to treat ADH1, that is designed to selectively antagonize the calcium sensing receptor (CaSR), targeting ADH1 at its source. Encaleret has received Fast Track Designation by the U.S. FDA and Orphan Drug Designation in the U.S., European Union, and Japan.

About BridgeBio Pharma, Inc.

BridgeBio Pharma, Inc. (BridgeBio) is a new type of biopharmaceutical company founded to discover, create, test, and deliver transformative medicines to treat patients who suffer from genetic diseases. BridgeBio's pipeline of development programs ranges from early science to advanced clinical trials. BridgeBio was founded in 2015 and its team of experienced drug discoverers, developers and innovators are committed to applying advances in genetic medicine to help patients as quickly as possible. For more information visit [bridgebio.com](https://www.bridgebio.com) and follow us on **LinkedIn**, **Twitter**, **Facebook**, and **YouTube**.

BridgeBio Forward-Looking Statements

This press release contains forward-looking statements. Statements in this press release may include statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), which are usually identified by the use of words such as "anticipates," "believes," "continues," "could," "estimates," "expects," "hopes," "intends," "may," "plans," "projects," "potential," "seeks," "should," "will," and variations of such words or similar expressions. BridgeBio intends these forward-looking statements to be covered by the safe harbor provisions of the Securities Act and the Exchange Act. These forward-looking statements include, but are not limited to, statements regarding BridgeBio's expectations for topline results from the Phase 3 CALIBRATE study of encaleret for ADH1, the potential for encaleret to become the first approved therapy for ADH1, and the planned initiation of a registrational study in chronic hypoparathyroidism in 2026. These statements reflect BridgeBio's current views about its plans, intentions, expectations, and strategies, which are based on information currently available and assumptions it has made. Although BridgeBio believes that its plans, intentions, expectations, and strategies as reflected in or suggested by these forward-looking statements are reasonable, it can give no assurance that they will be attained or achieved. Actual results may differ materially from those described in these statements due to a number of risks, uncertainties, and assumptions, including, but not limited to: the risk that topline results may be delayed or not yield positive outcomes; the risk that regulatory authorities may require additional data or studies; and the risk that encaleret may not be approved or commercialized. These risks also include impacts from global health emergencies, such as delays in regulatory reviews and disruptions to the global economy, as well as the effects of macroeconomic and geopolitical events, including hostilities in Ukraine and the Middle East, rising inflation, and fluctuating interest rates. Additional risks are described in the Risk Factors section

of BridgeBio's most recent Annual Report on Form 10-K, Quarterly Report on Form 10-Q, and other filings with the U.S. Securities and Exchange Commission. Moreover, BridgeBio operates in a competitive and rapidly evolving environment in which new risks may emerge from time to time. Except as required by applicable law, BridgeBio assumes no obligation to publicly update any forward-looking statements, whether as a result of new information, future events, or otherwise.

References

1. Dershem et al., Am. J. Hum. Genet., 2020.
2. Chang et al., Am. J. Hum. Genet., 2025.

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