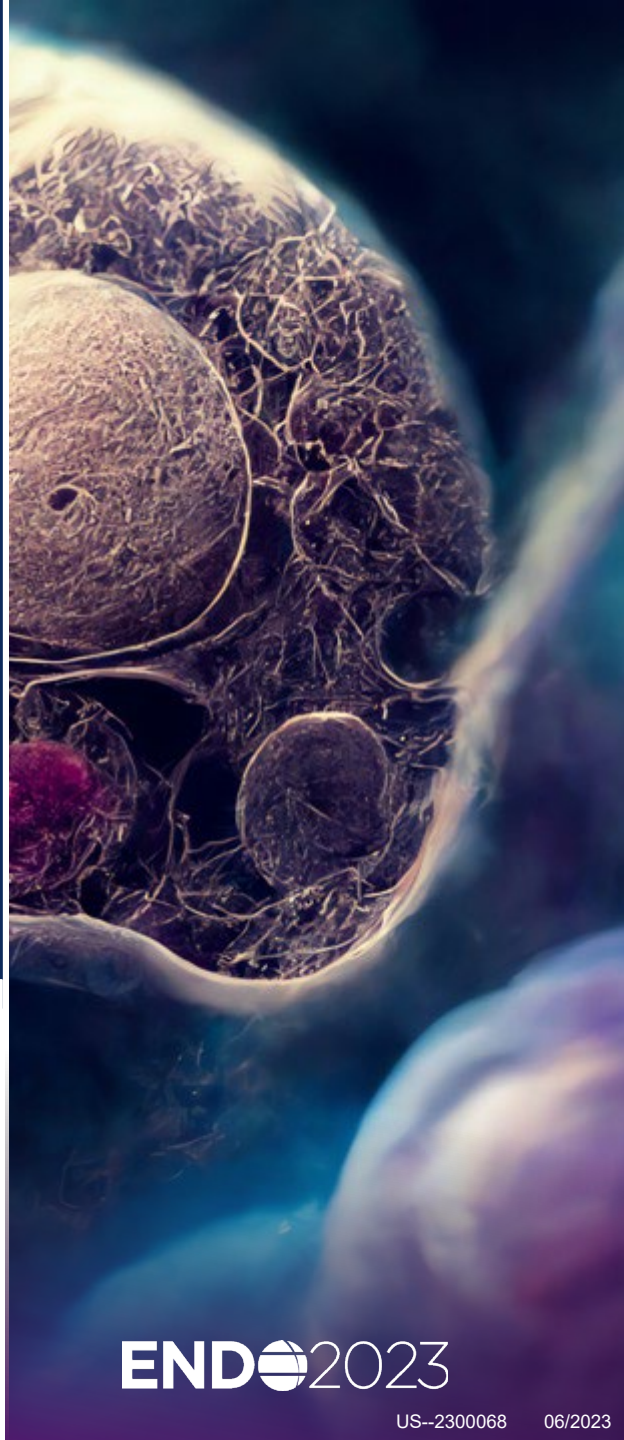
NEXT-GENERATION SEQUENCING FOR DETECTION OF UNDERLYING GENETIC CAUSES OF NONSURGICAL HYPOPARATHYROIDISM:

PRELIMINARY RESULTS FROM A SPONSORED TESTING PROGRAM



Prepared for presentation at the ENDO 2023 Annual Meeting

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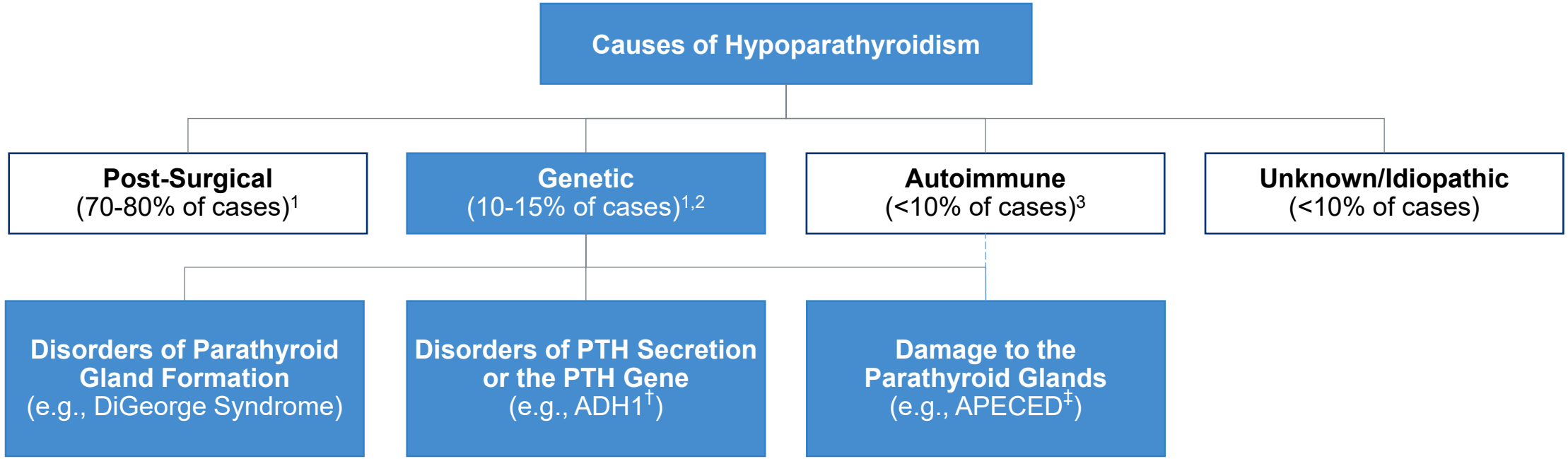
INTRODUCTION

Hypoparathyroidism (HP) is a rare condition characterized by inadequate production of parathyroid hormone (PTH) to maintain normal blood calcium levels



Genetic testing may uncover the underlying etiology of nonsurgical hypoparathyroidism
and can help confirm clinical diagnosis, guide medical management, and identify affected family members

†Autosomal dominant hypocalcemia type 1 (ADH1)
‡Autoimmune polyendocrinopathy with candidiasis and ectodermal dysplasia (APECED)
[1]Mannstadt, M et al. Nature Reviews Disease Primers, 2017; [2]Mannstadt M et al., ENDO Conference, 2023;[3]Bilezikian, JP et al., Jour Bone Miner Res., 2011

PROGRAM BACKGROUND

A sponsored genetic testing program using next-generation whole exome sequencing was made available at **no-charge** for patients with suspected genetic hypoparathyroidism who meet the eligibility criteria

PROGRAM ELIGIBILITY CRITERIA

The individual must reside in the US and meet any one of the following criteria:

- ☐ *Have a diagnosis of non-surgical/ idiopathic hypoparathyroidism*
- **OR**
- ☐ *Have a diagnosis of hypocalcemia suspected to be of genetic cause*
- **OR**
- ☐ *Have a relative with a diagnosis of genetic hypoparathyroidism*

26-GENE HYPOPARATHYROIDISM PANEL

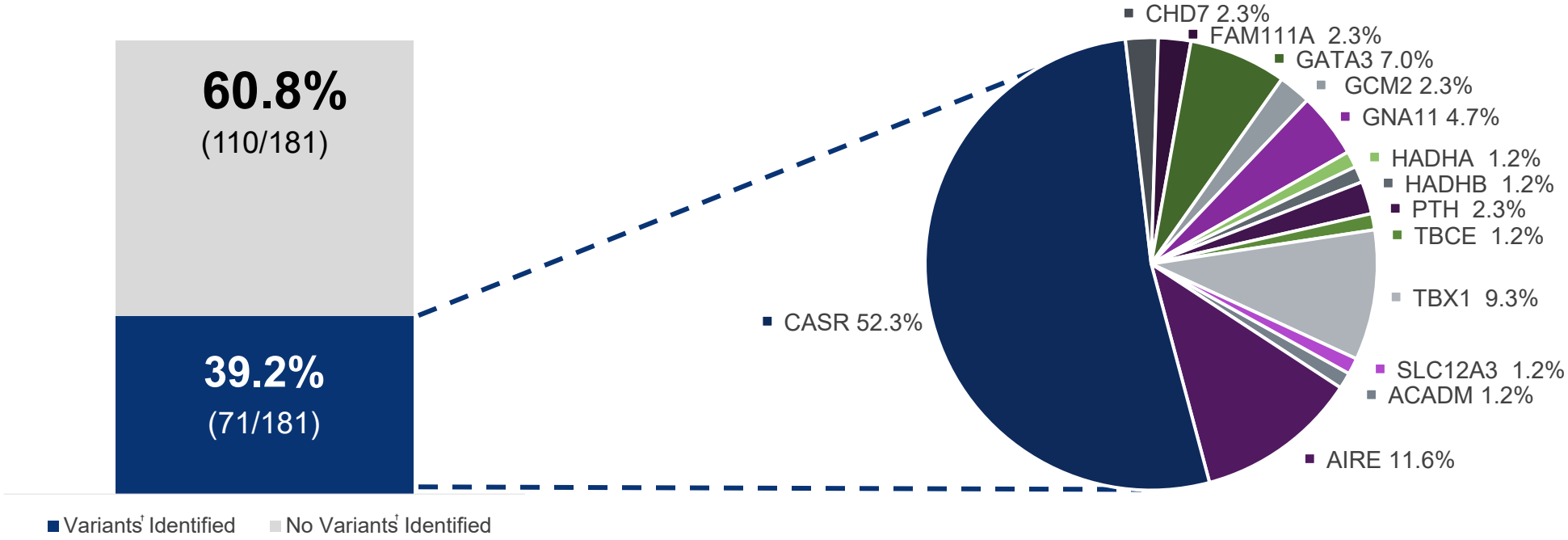
ACADM, AIRE, ATP1A1, CASR, CHD7, CLDN16, CLDN19, CNNM2, DHCR7, EGF, FAM111A, FXYD2, GATA3, GCM2, GNA11, HADHA, HADHB, KCNA1, NEBL, PTH, SEMA3E, SLC12A3, SOX3, TBCE, TBX1, TRPM6

PROGRAM START DATE
December 2020

DATA CUT
March 2023

RESULTS

- A total of **181 samples** were submitted from participants with a mean±SD age of 24.7±21.5 (range 0-81)
- **86 variants[†] were detected** in 71 individuals



- The most common genetic form of hypoparathyroidism was found to be autosomal dominant hypocalcemia type 1 (22.1% of individuals tested; 40/181), caused by gain-of-function variants in the CASR gene
- CASR variants[†] were found in more than half of the patients with identified variants[†] (52.3%; 40/71)

[†] Pathogenic, Likely Pathogenic and Variants of Uncertain Significance

CONCLUSION

- Genetic testing identified clinically-relevant variants[†] in approximately 2 of 5 individuals with nonsurgical hypoparathyroidism
- Genetic forms should be considered in all patients with hypoparathyroidism without history of neck surgery or other obvious causes; positive results can inform management of patients and suggest further medical work-up
- Autosomal dominant hypocalcemia type 1, resulting from gain-of-function variants in the CASR gene, emerged as the prevailing genetic cause of hypoparathyroidism; a confirmatory diagnosis may enable enrollment of eligible patients into an ongoing phase 3 clinical study [NCT05680818]
- Overall, this ongoing sponsored testing program will support the diagnosis of genetic hypoparathyroidism, and may ultimately improve patient management

No-Charge
Testing Kit

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[†] Pathogenic, Likely Pathogenic and Variants of Uncertain Significance